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# GENERAL SYMPTOMATOLOGY AND DIFFERENTIAL DIAGNOSIS OF DISSEMINATED SCLEROSIS *

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There is need for careful study of multiple sclerosis in all its aspects, clinical and pathologic. Above all, we must agree on its clinical limitations. If we succeed in establishing a definite concept of disseminated sclerosis, we shall help to clarify a number of other diseases of the central nervous system and their relation to the disease we are discussing.

Hitherto, there has been a wide divergence of opinion. Some have thought the disease rare; others that it is nearly as frequent as tabes. In this country the disease was at one time thought to be infrequent. In Japan, it is said to be practically unknown. On the other hand, Marburg [1] claimed that next to syphilis it is the most common organic disease of the nervous system, and Stieffler [2] has laid especial emphasis on the frequent occurrence of multiple sclerosis among German soldiers during the war. One group of authors has claimed that it is postinfectious—possibly a form of encephalomyelitis (Marie [3]). Others have contended that it is more often endogenous and degenerative (Strümpell and Müller [4]) or that it is endogenous and toxic (Oppenheim).[5]

Some of us were firmly convinced that multiple sclerosis is one of the few positively nonsyphilitic diseases of the central nervous system;

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* Read at the Meeting of the Association for Research in Nervous and Mental Diseases, Dec. 28, 1921.

* From the Neurological Service of Mount Sinai Hospital.

1. Marburg: Handbuch der Neurologie, Special Neurology 1, **2**:911, 1911.

2. Stieffler: Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:174, 1920.

3. Marie: Sclerose en plaques et maladies infectieuses, Progrès méd. **12**: 287-289, 305-307, 349-351, 365-366, 1884.

4. Strümpell and Müller: Einige Bemerkungen zur Aetiologie der multiplen Sclerose, Neurol. Centralbl. **115**:146-161, 1918.

5. A history of trauma was noted in only fourteen of our cases.

while others, including Spiller,[6] believed that syphilis may be an important factor in the causation of the disease.

Kuhn and Steiner [7] thought they had demonstrated the spirochetal origin of multiple sclerosis, and although this has been disproved by Rothfeld, Freund and Hornowski,[8] and has also been denied by Birley and Dudgeon,[9] the syphilitic origin of the disease has received some support from Schuster,[10] Gye,[11] Marinesco [12] and Siemerling.[13]

To my great surprise, I (Sachs) heard Pierre Marie say in Paris last summer that all cases of multiple sclerosis in patients above the age of 30 years were syphilitic in origin. Are he and we considering the same clinical entity?

Many observers in this country and Europe, more particularly in France, will not make the diagnosis of multiple sclerosis unless the classical triad of symptoms—nystagmus, intention tremor and scanning speech—is present; while others, like ourselves, venture to diagnose the disease in the presence of another series of symptoms, although one or two of the famous triad developed and emphasized by Charcot [14] and his followers, may be absent. As in tabes dorsalis, the earlier concepts of multiple sclerosis were based on the full fledged chronic forms of the disease, and as such the older clinical studies were keen and discriminating. The present day views, at least those which we hope to prove acceptable, are based on the attempt to recognize the disease in its earliest stages.

It is quite in order here to refer briefly to the fact that the older studies in the pathology of the disease differ from those of the present day, because the findings as reported years ago were concerned entirely with the later, and often with the terminal, stages of the morbid pro-

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6. Spiller: The Subacute Form of Multiple Sclerosis, Arch. Neurol. & Psychiat. **1**:219-230 (Feb.) 1919.

7. Kuhn and Steiner: Ueber die Ursache der multiplen Sklerose, Med. Klin. **13**:1007, 1917; Ztschr. f. Hyg. u. Infectionskrankh. **90**:417-422, 1920.

8. Rothfeld, Freund and Hornowski: Experimentelle Untersuchungen über die pathogenese der multiplen Sklerose, Deutsch. Ztschr. f. Nervenh. **67**:257, 1921.

9. Birley and Dudgeon: A Clinical and Experimental Contribution to the Pathogenesis of Disseminated Sclerosis, Brain **44**:150-212, 1921.

10. Schuster, J.: Beitrag zur Kenntnis der multiplen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **65**:1, 1921.

11. Gye: The Experimental Study of Disseminated Sclerosis, Brain **44**: 213-222, 1921.

12. Marinesco: Etude sur l'origine et la nature de la sclerose en plaques, Rev. neurol. **26**:481-488, 1919.

13. Siemerling: Spirochäten im Gehirn eines Falles von multipler Sklerose, Berl. klin. Wchnschr. **55**:273-274, 1918.

14. Charcot: Lectures on Diseases of the Nervous System, Series 2, London, 1881.

cess; whereas at the present time we are more interested in the beginning of the disease process. The older writers were concerned with the histology of the plaques, while the more recent group of investigators has attempted to determine the process leading to the development of sclerotic patches.

In view of the discrepancies just cited, it will be well to make a fresh start in the clinical study of the disease, neglecting for a moment the studies of Charcot, Marie, Oppenheim,[15] Strümpell, Müller, Taylor,[16] Spiller and Jelliffe,[17] and wholly disregarding a critical digest of the disease which Sachs [18] published in 1898, except to say that many of the problems confronting us today were recognized and stated by the writers of several decades ago.

## FREQUENCY OF DISSEMINATED SCLEROSIS

Our own studies are based on a series of 141 cases. Ninety-one cases were observed in the neurologic service at Mount Sinai Hospital during a period of ten years, from 1912 to 1921 inclusive, and fifty cases at the Montefiore Hospital for Chronic Diseases. Figures demand interpretation. The Mount Sinai service is essentially an "acute" service. The hospital stay of any patient is supposed to be limited to a period of six weeks.

TABLE 1.—TOTAL ADMISSIONS TO THE NEUROLOGICAL SERVICE, TWO THOUSAND THREE HUNDRED AND FIFTY-SEVEN PATIENTS

| Disease | Cases | |
|---|---|---|
| Multiple sclerosis | 91 | ( 3.9%) |
| Syphilitic affections of the central nervous system | 562 | (23.8%) |
| Of these: | | |
| Cerebrospinal syphilis | 317 | |
| Tabes dorsalis | 160 | |
| General paresis | 85 | |

During this entire period we did not encourage the admission of patients suffering from multiple sclerosis. We did encourage the admission of patients with syphilitic affections, and yet our records show that multiple sclerosis was more than half as common as was tabes dorsalis and fully as frequent as general paresis—the last, like

15. Oppenheim: Zur lehre von der multiplen Sklerose, Berl. klin. Wchnschr. **33**:184-189, 1896.

16. Taylor: Multiple Sclerosis: A Contribution to Its Clinical Course and Pathological Anatomy, J. Nerv. & Ment. Dis. **33**:361-406, 1906.

17. Jelliffe: Multiple Sclerosis. Its Occurrence and Etiology, J. Nerv. & Ment. Dis. **31**:446-455, 1904.

18. Sachs, B.: On Multiple Sclerosis with Special Reference to Its Clinical Symptoms, Its Etiology and Pathology, J. Nerv. & Ment. Dis. **25**:314-331, 464-478, 1898.

multiple sclerosis, being observed as a rule in its earliest stages. In this group the incidence of the disease is understated, a very large proportion of patients with multiple sclerosis not requiring hospital treatment.

The smaller group of the Montefiore Hospital is classified in Table 2.

TABLE 2.—Admissions to the Montefiore Hospital

| Disease | Cases |
|---|---|
| Multiple sclerosis | 50 |
| Syphilitic affections of the central nervous system | 167 |
| Of these: | |
| Cerebrospinal syphilis | 65 |
| Tabes dorsalis | 85 |
| General paresis | 17 |

In this institution for chronic diseases, in which there was no reason to give preference to any special group, the proportion of disseminated sclerosis to tabes is as 5 to 8.5.

We note that of the 141 patients, 100 were between the ages of 20 and 40 years.[19]

## SIGNS AND SYMPTOMS OF THE DISEASE

In the study of the signs and symptoms of disseminated sclerosis, I (Sachs) was most anxious to avoid the dangers that lurk in statistics. For that reason I constructed from my own clinical experience and impressions Table 3. The percentages were added later as the result of Dr. Friedman's careful analysis of the hospital records. May I add at once that the diagnostic importance of a symptom is not always to be measured by the frequency of its occurrence? For instance, unusual remissions, or disturbances of vesical control, may be noted more frequently than pallor of optic disks, and yet the diagnostic importance of the latter is far greater than that of the former.

Without wishing to encroach on the topics assigned to others, let us dwell briefly on a few of the more important signs and symptoms. Let us also assume that the majority of the facts here adduced are known to, and conceded by, all.

First, it is of special interest to note the gradual development of the weakness, as a rule in the lower extremities, in association with increase of the deep reflexes.[20] The upper extremities are less frequently involved in the general loss of power, while a slight ataxic tremor[21]

19. Second decade eight cases, third decade forty-seven cases, fourth decade fifty-three cases, fifth decade twenty-five cases, and sixth decade five cases. These figures do not accurately account for the age of onset.

20. In 115 cases the chief complaint was weakness and stiffness of one or both lower extremities.

21. Cerebellar ataxia and adiadokokinesis were noted in sixty-six cases, showing the frequent involvement of cerebellar pathways.

often precedes by months the development of weakness or paralysis of the upper extremities, and the upper extremity reflexes are increased at an early day. In both the upper and lower extremities weakness or paralysis is associated with a moderate degree of spasticity; not infrequently there is also in the early stages of the disease a slight though distinct disturbance of sensation.[22]

TABLE 3.—SIGNS AND SYMPTOMS OF MULTIPLE SCLEROSIS IN THE ORDER OF THEIR DIAGNOSTIC IMPORTANCE. BASED ON THE STUDY OF ONE HUNDRED AND FORTY-ONE CASES

| | Percentage |
|---|---|
| 1. Easy fatigue, weakness and stiffness of one or both upper or lower extremities culminating in spastic paraplegia | 81.7 |
| Associated with | |
| Increase of deep reflexes | 90 |
| Positive Babinski sign | 78.3 |
| 2. Nystagmus, generally horizontal, slight at the beginning, gradually becoming more marked | 70 |
| 3. Ataxic tremor of upper extremities and tremor of the head | 55.3 |
| 4. Marked diminution or loss of abdominal reflexes | 83.7 |
| 5. Spastic ataxic or ataxic gait and station (including the Romberg symptom) | 43.2 |
| 6. Scanning speech or some form of dysarthria | 36 |
| 7. Pallor of optic disks, especially of the temporal halves | 32.6 |
| 8. Disturbance in facial innervation, often slight | 32.6 |
| Deviation of tongue, 10% | |
| Disturbance of deglutition, 3.5% | |
| 9. Explosive laughter and emotional instability | 17 |
| 10. Unusual remissions often leading to disappearance of symptoms | 42 |
| 11. Transitory ocular palsies with diplopia | 29 |
| 12. Vague objective and subjective sensory disturbances: | |
| Objective: (1) Posterior column disturbance | 17 |
| (2) Pain, touch and temperature disturbance | 16.3 |
| Subjective: Numbness, tingling and pain | 30 |
| 13. Disturbance in vesical (not rectal) reflexes | 40 |
| (Hasty or delayed micturition); incontinence in 21 cases, 14%) | |
| 14. Tenderness of the spine, chiefly mid-dorsal | 12 |
| 15. Dizziness (vestibular vertigo) | 8¼ |
| 16. Mental changes | 15.6 |
| 17. Auditory nerve involvement | 2 |

IMPORTANT NEGATIVE SIGNS AND SYMPTOMS

1. Pupils generally active with occasional hippus.
2. Biologic tests negative except for the occasional presence of globulin and slight increase in the number of cells in the spinal fluid in a few instances.

The fact that the disease patches occur at various levels in the pyramidal tracts and in the cerebellar pathways accounts for the character of the motor symptoms and also for the easy division into special types in accordance with the topographic distribution of the lesions. If we choose, we may establish spinal, bulbar, cerebral, hemiplegic and cerebellar types.

22. Astereognosis was noted in five cases, possibly accounting for the "loose arm" referred to by various writers.

The disease process and the disease symptoms are widespread. Of the increase of the deep reflexes [23] little need be said, except that it is within moderate bounds, that it is generally equally and symmetrically distributed over the entire body, and that in many instances the jaw reflex is very active, as evidence that the sclerotic patches may be distributed throughout the length and breadth of the central nervous axis.

The diminution or loss of the abdominal reflexes is the one symptom of importance that has been added to the symptomatology of multiple sclerosis within the last twenty years. We have been forced to attach great significance to it, yet it is only fair to state that some French authors, like Marie and Sézary,[24] are inclined to disregard the value of this reflex.

In many instances the absence of the abdominal reflex has led us to suspect the presence of disseminated sclerosis early in the disease, the suspicion having been confirmed by subsequent developments. How can we account for the frequent loss of this reflex? Except at the beginning of the disease, all abdominal reflexes seem to be equally affected. I find no explanation except that in view of the extensive character of the disease, the reflex pathways with their cerebral connections are certain to be hit somewhere by one or more of the sclerotic patches; and this view is substantiated by Monrad-Krohn,[25] a Scandinavian writer, who in a recent and exhaustive monograph on the abdominal reflexes says that these reflexes are present in all healthy persons with normal abdominal walls, and that there is a pathway connecting the spinal arc with the sensorimotor cortex.

So far as the speech disturbances are concerned, scanning speech does not tell the whole story. In addition to or instead of syllabic utterances we may have other forms of dysarthria. Speech may be purely tremulous or bulbar or cerebellar in character.

Ever since Uhthoff's [26] day, the pallor of the temporal half of the optic disks [27] has had great diagnostic value, and, last but not least, the unusual remissions of the disease often afford great difficulty in diagnosis. Sometimes men of experience doubt the diagnosis because

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23. Ankle clonus was present in sixty-one cases; patellar clonus in twenty-nine cases. The knee reflexes and the Achilles reflexes (tabic type), were diminished in three cases.

24. Sézary: Traite de pathologie médicale et de therapeutique appliquée, Neurologie **1**:338.

25. Monrad-Krohn: On Abdominal Reflexes, Norsk Mag. f. Lægevidensk. **79**:1918, supplement to December number (English summary).

26. Uhthoff: Untersuchungen über die bei multipler Herdsklerose vorkommenden Augenstörungen, Arch. f. Psychiat. **21**:303-410, 1890.

27. Expert ocular examination revealed "blurring of the disks or mild optic neuritis" in eleven cases. Vision was found "impaired" in twenty-five cases without objective disk findings.

of the disappearance of many signs. The gait improves, the speech becomes less scanning, the contractures are partially relaxed, the ataxic tremor of the upper extremities may be far less pronounced. Great subjective improvement is reported by the patient, and the general progress is so marked that not infrequently hysteria or some functional form of disease [28] is suspected. The diagnosis of multiple sclerosis may safely be made if a number of the important symptoms enumerated in Table 3 are present, and if the disease runs a subacute or chronic course.[29]

### DIFFERENTIAL DIAGNOSIS

The textbooks give a long list of diseases from which multiple sclerosis is to be differentiated. The list includes paralysis agitans, tumor and pseudotoumor of the brain (especially in the cerebellar pontile angle), and of the spinal cord, general paresis, hysteria and many other conditions. We may safely leave the consideration of these to the textbooks.

There is one differential diagnosis of paramount importance, and to that it will be well to give full consideration. Is the patient suffering from multiple sclerosis or from multiple cerebrospinal syphilis? In both diseases the patients have in the course of a few months or possibly a few years developed from slight beginnings a more or less marked spastic weakness of the lower extremities associated with increase of all the deep reflexes. In both diseases there are marked periods of remission and of exacerbation. Personally, I have seen the remissions just as marked in the one disease as in the other.

In cerebrospinal syphilis there are pupillary symptoms and ocular palsies that point indubitably to the constitutional infection, and there are in the majority of instances positive biologic findings: a positive Wassermann reaction in the blood and in the spinal fluid with increase in globulin and in the number of cells. In disseminated sclerosis we have pronounced nystagmus, transitory ocular pareses, more or less marked intention tremor, as well as spastic contracture of the limbs. To be sure, there are also cases of cerebrospinal syphilis in which nystagmus occurs and in which there may be slight ataxia or ataxic tremor of the upper extremities. If there is distinct syllabic or scanning speech the diagnosis of disseminated sclerosis is obvious.

But the difficulty is that there are also some cases of cerebrospinal syphilis in which there may be a more or less marked dysarthria, bulbar

28. We have noted distinct mental changes in only twenty-two patients, exclusive of those with emotional instability and explosive laughter. A childish attitude toward their illness and a certain degree of euphoria have been noted.

29. Marburg's substitute triad, afebrile course, multiplicity of foci and unusual remissions, is not sufficiently definite for diagnostic purposes.

or cerebellar in type. The two groups approach each other so closely that in not a few instances it is well nigh impossible to state definitely from which one of the two diseases the patient is suffering; but there are a few differential signs of great importance.

First and foremost, in disseminated sclerosis the pupillary reactions are almost universally normal, whereas in fully 90 per cent. of cases of cerebrospinal syphilis immobility of the pupils is an early and constant symptom. If there is an irregular contour of the pupils as well, the suspicion of a syphilitic disease is fully corroborated. The ocular palsies in syphilis are early and complete—in multiple sclerosis they are partial and transitory. In disseminated sclerosis the serologic findings are practically negative; in cerebrospinal syphilis they are, as a rule, positive enough to confirm the diagnosis.

There is one other condition of great significance. The spasticity in cerebrospinal syphilis is greater than in disseminated sclerosis unless the patients are in or near the terminal stage of the disease. In the early stages of disseminated sclerosis there is weakness and only a slight degree of spasticity. In cerebrospinal syphilis there is marked spasticity and relatively less weakness. As Erb pointed out years ago, the rigidity of the patient with spinal syphilis is excessive. He could go about easily if there were not inordinate spasticity of gait. The average patient suffering from multiple sclerosis has in the first years of his illness a weakness which becomes more and more pronounced, but spasticity is far less marked than paresis. Even so, there are further difficulties. May not disseminated sclerosis occur in a person suffering from constitutional syphilis who may, therefore, present immobile pupils and slightly positive serologic findings? But if he has a number of the other important symptoms of disseminated sclerosis, are we not justified in diagnosing multiple sclerosis in a person suffering from constitutional syphilis rather than cerebrospinal syphilis pure and simple? Furthermore, if the serologic findings are negative [30] and the pupils are not completely immobile, the diagnosis of cerebrospinal syphilis is doubtful, although the majority of symptoms point to syphilitic affection rather than to disseminated sclerosis.

These differences are emphasized by the fact that excessive spasticity or spasticity far greater than the paresis argues in favor of the syphilitic infection. Immobility of pupils and positive biologic findings help to corroborate this diagnosis. Slight spasticity, normal pupillary reactions, negative findings and the presence of other positive signs, will lead to the diagnosis of disseminated sclerosis.

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30. The spinal fluid was negative in 114 of 122 cases studied. The spinal fluid Wassermann test was negative in all these cases. In eight cases the cell count was above normal, the figures being 12, 13, 16, 16, 20, 30, 30 and 40 cells, respectively. In three cases the globulin was increased.

ILLUSTRATIVE CASES

To illustrate the difficulties of the diagnosis, the symptoms in two cases will be presented briefly. The first is taken from private practice, but has not been included in our list, as we have excluded all private cases because in the nature of things they cannot be studied as thoroughly as are the hospital cases.

A man, now 39 years of age, has been under observation for two years and three months. At first he complained chiefly of a feeling of weakness in the knees and right foot when walking. He had been married for sixteen years and had four healthy children. A papilloma of the left vocal cord had been removed eight months before his first visit. He had a chronic nasopharyngitis. Lumbar puncture had been performed and the findings had been negative. The Wassermann test of the blood and of the spinal fluid was negative. He had a slightly spastic gait; all the deep reflexes were exaggerated. There was a slight suspicion of speech disturbance, although the patient himself asserted that his speech was normal.

At first there was distinct improvement under treatment with cacodylate injections. There was no intention tremor. He had perfect control over his vesical and rectal reflexes. His pupils reacted well; there was slight nystagmus. During the year 1920 the spasticity was much lessened, but beginning with the spring of 1921 there was a marked return of weakness of the legs and the spasticity had become extreme, so that now he has great difficulty in mounting stairs or in getting into an automobile. His pupils, however, are entirely normal; the Wassermann reaction of the blood remains negative; the abdominal reflexes are active; there is no marked disturbance of speech; there is little intention tremor and slight nystagmus.

We have been inclined, however, to regard this patient's condition as disseminated sclerosis, but the presence of the abdominal reflexes and the inordinate spasticity make it doubtful whether the case may not be one of cerebrospinal syphilis in spite of the normal pupils and the negative serologic findings. Were Pierre Marie to see this patient, he probably would feel justified in saying that he was suffering from cerebrospinal syphilis. There is some comfort in knowing that there are relatively few cases that present as marked difficulties as does this one.

In the second case the symptoms were briefly:

A clerk, aged 38, born in the United States, admitted Jan. 30, 1918, had a fall eleven years before his admission to the Home and since this accident he has been unable to get about. The records show: weakness and trembling of the legs, urgency of urination, marked exaggeration of all the deep reflexes, including a double Babinski sign; the abdominal reflexes were more feeble on the right; the cremasteric reflexes were absent; speech was hesitant; the patient had had a number of convulsions, the first seizure at the age of 22. It was stated that the head was tilted to the left; there was temporal pallor of the disks; the spinal fluid was normal; there was disturbance of sensation in the toes; the retina showed a picture of syphilitic degeneration; the right

pupil was larger than the left and it reacted sluggishly; there was lateral nystagmus; weakness of the left side of the face; weakness of the right grip; loss of muscle sensation in the upper extremities; head tremor; ataxia, and tremor in both hands. There were also uncontrollable laughter, a double Babinski sign, and all the abdominal reflexes, except the upper left reflex, were absent. The Wassermann test was negative in the blood and in the spinal fluid.

Death was sudden. The postmortem examination revealed a primary idiopathic internal hydrocephalus, multiple sclerosis and pachymeningitis. There was thickening of the pia-arachnoid and marked enlargement of the ventricles. The ependyma was thickened; the spinal cord was markedly diminished in circumference and showed degeneration of the dorsal tracts and crossed pyramidal tract on the right side.

Clinically this patient presented the symptoms of multiple sclerosis with a suspicion of constitutional syphilis, and we would interpret the report of the pathologist in the same way—a combination of sclerotic plaques and a chronic syphilitic process.

### COMMENT

In summarizing the clinal studies, let us again suggest that the diagnosis of disseminated sclerosis is warranted in the presence of a combination of any number of the important signs enumerated in Table 3, particularly if corroborated by the entirely negative character of the pupillary reactions and of the biologic tests.

That there will be occasional pitfalls and errors may be conceded, but that is practically as true of disseminated sclerosis as it is of all other organic diseases of the central nervous system.

# MULTIPLE SCLEROSIS: THE LOCATION OF LESIONS WITH RESPECT TO SYMPTOMS*

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Assuming that multiple sclerosis, as ordinarily understood, represents a definite disease entity having a characteristic pathologic anatomy, a correlation of signs and symptoms with lesions should be possible as in other disorders of recognized organic character. Certain difficulties, however, at once present themselves; first, owing to the relatively nondestructive character of the pathologic process, no just parallel can be drawn between its apparent extent and the resultant signs and symptoms; in the second place, exact and painstaking correlations of lesions and symptoms have rarely been attempted in the now large number of clinically observed cases with subsequent necropsy. Most writers have been content with general statements regarding pathologic findings as explanatory of symptoms, as, for example, numerous cortical areas of sclerosis, or many sclerotic patches in the pons or oblongata or the cord showing plaques in both sensory and motor tracts. The reason for this apparent inaccuracy is sufficiently obvious. A disease process which manifests itself pathologically by perhaps a hundred or more lesions scattered indiscriminately throughout the central nervous system cannot adequately be described or pictured. Owing to the peculiarity of the pathologic alteration, also, even if its geography could be accurately mapped, the correspondence between lesion and symptom would still be so vague as to be of comparatively little physiologic value. In many cases there appears to be practically no relation between the symptoms observed during life and the findings postmortem. As the necropsies have multiplied it has become increasingly apparent that a very large number of cases unsuspected during life have been demonstrated to be multiple sclerosis of typical pathologic character. This fact alone doubtless accounts for what has always seemed to me an erroneous assumption that multiple sclerosis was a rare disease and less frequent in this country than in Europe. In view of our increasing knowledge the assumption that perhaps next to tabes, multiple sclerosis is the most frequent organic disease of the nervous system, may not be an over-statement.[1] The so-called formes frustes of Charcot are

* Presented at a meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 28, 1921.

1. Marburg agrees with Müller and Schultze regarding multiple sclerosis as the most frequent organic nervous disease except syphilis. Lewandowsky: Handbuch der Neurologie **2**:916.

certainly far more frequent than the classical type of the disease,[2] and presumably few would now agree with the statement made by Sachs[3] in 1898 that the diagnosis should not be made in the absence of the so-called cardinal symptoms.

In the analysis which follows an attempt will be made to proceed from the more general correlations to the more specific localizations so far as that is possible. However divergent the symptoms may be from the picture first drawn by Charcot,[4] we still recognize a type form of the disease characterized by nystagmus, scanning speech and ataxic tremor of the intention type to which may be added weakness with spasticity. This well defined combination of signs occurs in no other condition in like degree. The nystagmus, volitional tremor and speech defect may be regarded as due in some measure, at least, to the peculiar character of the lesion as well as to its location. The early loss of myelin and persistence of axons and cells must be held at least in part responsible for these characteristically irregular movements. Charcot[5] definitely regarded this irregularity of movement as conditioned by an altered resistance to conduction in the sclerotic area. If the myelin may be considered as in some sense an insulating mechanism, as pointed out particularly by Porter E. Sargent,[6] a possible partial explanation of the incoordination is found. Erb, on the other hand, believed it due rather to the localization of the sclerotic patches than to any peculiarity of the pathologic process itself, a theory which has gained in acceptance as the general knowledge of localization has increased. Dawson,[7] for example, considers the hypothesis established that the incoordination results from interruption of, or disturbance in, the cerebello-rubro-thalamo-cortical pathway. As this pathway, because of its wide extent,

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2. Classical type, Müller, 15 per cent.; Marburg, even less; Aschern, three cases out of twenty-five, 12 per cent.

3. Sachs: J. Nerv. & Ment. Dis. **25**:325, 1898. At the meeting at which this paper was presented Dr. Sachs said that he had changed his opinion regarding the diagnostic criteria of the disease.

4. Charcot: Lectures on Diseases of the Nervous System, English translation by Sigerson, New Sydenham Society, 1877. Although written nearly fifty years ago, this lecture still stands as perhaps the best description of the disease.

5. Charcot: Lectures on Diseases of the Nervous System, p. 218: "The long persistence of the axis-cylinders, deprived of medullary sheathing in the midst of the foci of sclerosis, probably plays an important part here. The transmission of voluntary impulses would still proceed by means of the denuded axis-cylinders, but it would be carried on irregularly, in a broken or jerky manner, and would then produce the oscillations which disturb the execution of voluntary movements."

6. Unpublished research.

7. Dawson: Rev. Neurol. & Psychiat. **15**:146, 1917. For a detailed account of various theories see Müller: Die multiple Sklerose des Gehirns und Rückenmarks, Jena, 1904, p. 115.

is altogether likely to be involved in some part of its course, secondarily affecting the innervation of the corticospinal and spinoperipheral motor tracts, an explanation of the tremor both of arms and legs is established as well as of the speech mechanism.[8] The eye muscle involvement leading to nystagmus is likewise regarded as due to lesions about the ventricle, aqueduct, third nerve nucleus, Deiters' nucleus and doubtless higher levels as well. The tendency to spasticity with or without hypertonicity is naturally explained by an invasion of the pyramidal tracts somewhere in their long course. If such a theory be valid, it naturally presupposes lesions in these regions when the classical type of the disease appears. It follows, if such lesions do not occur, that the typical picture of the disease is lost in a wide range of symptoms due to lesions otherwise localized.

The attempt to follow these so-called formes frustes[9] in all their ramifications is obviously impossible. Before even attempting to particularize, it should be understood that symptoms of the most varied sorts, many of them quite impossible of explanation, may occur which, as shown by postmortem findings, must in some way be attributed to sclerotic patches of the kind under consideration. It is also a well demonstrated fact that many lesions are discovered at necropsy which gave no recognized sign of their existence during life, notably in the brain stem involving the cranial nerve nuclei and fibers.

As before stated, it is futile to attempt an exact determination of symptoms from lesions, or of lesions from symptoms, as is possible in other organic disorders, in which nerve elements are completely destroyed. Admitting this important source of error, the general principles of localization apply in this as in other diseases. Considered first from the symptomatic standpoint, the original group of symptoms —nystagmus, scanning speech and intention tremor—find their explanation presumably in lesions of the thalamus and its cerebellar connections, although the peculiar character of the pathologic process (myelin degeneration) must still be given some consideration. This group of symptoms occurs in a relatively small percentage of the cases. The bewildering number of symptoms common to this and other organic and even functional diseases may in a general way be explained by the multiplicity and irregular distribution of the lesions.

Charcot explained the ataxia and pain by invasion of the dorsal tracts, muscular atrophy by destruction of ventral horn cells, spasticity

8. Probst: Deutsch. Ztschr. f. Nervenh. **12**:446, 1898. Probst describes a case in which there was neither intention tremor nor nystagmus in spite of extensive lesions in the pons, quadrigeminal region and dorsal longitudinal bundle.

9. Charcot: Des formes frustes de la sclérose en plaques. Clinique des maladies du systéme nerveux, Paris, 1892, p. 399.

by involvement of the lateral tracts, nystagmus and difficulty of speech by lesions in the pons and oblongata, etc. Such general statements are obviously unassailable. The difficulty arises in the more minute correlations.

Somewhat dogmatic deductions are given as follows by Dawson: Symptoms in his case began with a weakness of the legs, passing off, recurring, growing rapidly worse and terminating in a spastic paraplegia. "This is obviously the clinical manifestation of the dense areas of sclerosis which were found throughout the spinal cord." These from their histologic appearance apparently were the earliest manifestations of the disease. The same was true of lesions found in the sacral region which were regarded as responsible for the patient's sphincteric difficulties. The volitional tremor which next developed is associated with patches in the superior cerebellar peduncle, red nucleus and optic thalamus. The nystagmus, an early symptom, was "undoubtedly associated with the periventricular and periaqueductal sclerosis, only parts of the oculo-motor nerves being involved." Patches in the cervical region are assumed to cause sudden numbness in the left arm followed by rapid development of large areas in the pons involving the eighth nerve producing deafness, and in the facial nucleus producing a right facial paralysis. Later a patch involved the sixth nucleus leading to diplopia from external rectus paralysis. Soon patches involved the twelfth nerve and nucleus leading to protrusion of the tongue to one side with slight trouble with speech and swallowing; dimming of vision followed by total blindness the next morning "was obviously the result of the development of patches in the optic tracts and chiasm." Finally, it is assumed that the areas in the cord became more extensive, involving the lower motor neurons and resulting in muscular wasting and emaciation. This observation is of interest since Dawson has been able to determine the age of lesions by their microscopic appearance, but even so the extent of his assumption is hardly justified.

It may be said without fear of contradiction that the frequent, if not universal, mental disturbances are due in large measure to cortical lesions, that the relatively slight but practically constant sensory defects are due to lesions in the cerebrospinal sensory tracts, and that the conspicuous motor phenomena result from interference with the motor conduction paths. One is, however, by no means justified in assuming in any given case that the cortex alone is involved in the mental disorder, or that sensorimotor signs are dependent on lesions in any one portion of the afferent and efferent tracts. In the attempt to explain the frequency of certain symptoms Brouwer [10] has advanced an ingenious hypothesis from the biologic and developmental standpoint, which is worthy of serious consideration.

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10. Brouwer: The Significance of Phylogenetic and Ontogenetic Studies for the Neuropathologist, J. Nerv. & Ment. Dis. **51**:113, 1920.

He believes that it may be possible to explain the chief symptoms of the disease through an appeal to evolutionary principles. The usual statement that the frequency of spastic conditions is due to an affection of the pyramidal tracts because these tracts are longer and therefore more exposed, he regards as unsatisfactory. He, furthermore, does not agree with the generally accepted idea that sensory fibers are more resistant than motor fibers, hence the slight disturbance of sensibility. He also asks how it can be that in spite of its variety of manifestation, a certain definite group of symptoms still dominates the clinical picture. To meet these various objections and to consider the symptoms from a unitary standpoint, he appeals to the phylogeny of the nervous system. Reference is made to the following clinical examples in the attempt to establish his contention:

A patient with merely a slight paresis of the left facial nerve was almost totally unable to speak. The brain stem was much involved in the sclerotic process, both the nuclei of the cranial nerves and their roots. Why, he asks, can such a patient not speak while showing practically no changes in the function of the cranial nerves in general? In a second instance he refers to loss of the abdominal reflexes. Why, again, is the nystagmus almost invariably horizontal? If due to foci in the oblongata, why are other cranial nerves not involved? In a case of practically complete transverse lesion of the thoracic cord the legs may be almost totally paralyzed, whereas the sensory disturbances are usually relatively slight. Finally, why is the temporal half of the optic disk paler than the nasal half when apparently the entire nerve at some part of its course is sclerotic? A reconciliation of these difficulties is attempted.

Presupposing, as Brouwer believes justified, that multiple sclerosis is due to an infective agent of some kind, it is a fair assumption that the older parts of the nervous system have greater resistance to such agents than the phylogenetic and ontogenetic younger parts which naturally represent the higher, more developed functions. Reverting to the previous examples, the function of speech is a late development, whereas the cranial nerve tracts are for the most part archaic. Hence, lesions apparently affecting this whole area, in common, involve speech in a maximum degree. Again, the abdominal reflex occurs only in primates, hence it likewise is a late phylogenetic development and is therefore lost early. The horizontal nystagmus is brought into relation with the fact that the side movement of the eyes in the horizontal plane is present only in higher mammals on account of the position of the eyes in front of the head. Here, again, the same principle applies. That the disturbances of motility are greater and more frequent than those of sensibility is due to the fact that the pyramidal tracts are young,

both from the racial and individual standpoint.[11] The cerebrocerebellar tracts in the pons are conspicuously developed in the higher mammals and particularly in man; therefore there is a frequency of disturbed coordination, since these tracts, developed late, are often involved in the sclerotic process. Finally, the much discussed temporal pallor of the disk (symptom of Uhthoff) finds its explanation in the imperfect crossing of the optic fibers in the mammalia, including man. Phylogenetically, the temporal half of the disk is the younger; hence, according to the theory, it suffers more in the pathologic process than does the nasal side.[12] The well recognized mental changes are naturally explainable on the same basis.

From such arguments as this Brouwer adduces the general principle that the causative agent in the disease damages younger and later developed functions much more definitely and persistently than older and more primitive functions. It is reasonable to suppose that higher developed functions should first succumb to a partially destructive lesion, such as that of multiple sclerosis. Brouwer appears to have made out his case, that the "fundamental" symptomatology runs parallel with both the phylogenetic and ontogenetic development of the nervous system, in the sense that the so-called cardinal symptoms and certain others frequently encountered result from functional disturbance in the tracts later developed. The theory, however, is difficult of application in relation to the signs and symptoms which multiple sclerosis shows in common with other forms of organic and functional disease.

### MULTIPLE SCLEROSIS FROM THE ANATOMIC STANDPOINT

Considered from the anatomic standpoint, the (1) cortex, centrum ovale, (2) basal ganglions, (3) cerebellum, (4) optic system, (5) brain stem and cranial nerves, and (6) cord, may with advantage be considered separately.

*The Cortex.*—Sclerotic areas in the cortex were slow of recognition. Their presence was definitely established in the early nineties, although even as far back as 1869, a sketch by Charcot,[13] pictures lesions in the cerebellar cortex but apparently not in the cerebral cortex. That very numerous plaques may occur throughout the cortex is no longer open to question. The relation of such alterations to the frequent mental changes in the disease may in general be accepted, although naturally

11. Late myelinization.

12. Early degeneration of the maculopapillary bundle has also been assigned as a cause of the temporal pallor, but this in no way controverts Brouwer's theory. He, naturally, does not confine his deductions to multiple sclerosis.

13. Bourneville and Guérard: De la sclérose en plaques disséminées, Paris, 1869. Valentiner associated mental changes with involvement of the "subtsance of the central hemispheres."

it is quite impossible to associate definite symptoms of impairment with definite lesions. Raecke [14] discusses the mental changes as observed up to 1906 but with very general pathologic observations in only one case. A later monographic article by Siemerling and Raecke [15] on the basis of eight cases with necropsies makes very general reference to the psychic changes in reference to the lesions. For example, in one case (Case 8 of the series) during life there was euphoria passing over to increasing dementia with changes of mood and grandiose ideas. Postmortem lesions, larger and smaller, were found in the cerebral cortex and white matter, many of them microscopic, with general brain atrophy. No further correlation is attempted. In other cases characterized by euphoria, similar vague statements are made regarding numerous areas in the cortex, but without further definition. It is clear from these and many similar observations that no exact correlation is possible between symptoms and lesions affecting the cortex, and that the cortex may be extensively involved without corresponding mental disturbance. No more exact statement can at present be made than that the cortex is frequently involved in the sclerotic process and that mental symptoms usually of the type of a progressive but not extreme dementia [16] are somewhat characteristic. In this connection Müller warns against drawing the deduction that extreme mental disorder corresponds to the number and extent of cortical lesions.[17] Our knowledge of the relation of mental processes to brain structure is far too vague to permit any deductions of value, especially in the disease under consideration, with the complicating existence of lesions in other and diverse areas of the brain.

The association of multiple sclerosis with dementia paralytica is of interest. Hunt,[18] in 1903, reviewed seven cases of this type, giving the necropsy findings in six, and added a detailed report of a personal case in which he found extensive cortical changes, alteration of cells,

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14. Raecke: Arch. f. Psychiat. **41**:482, 1906. Duge: Deutsch. Ztschr. f. Nervenh. **51**:459, 1914.

15. Siemerling and Raecke: Arch. f. Psychiat. **53**:385, 1914. Bibliography 441 titles, 158 cuts.

16. Seiffer: Arch. f. Psychiat. u. Nervenk. **40**:252, 1905, characterizes this disturbance as a "polysclerotic dementia," the peculiarities of which are euphoria and frequent and sudden change of mood, for long periods standing in no definite relation to the usually slight degree of dementia. Other more pronounced symptoms may occur running the gamut of the entire psychic symptomatology. In certain cases the association with dementia paralytica should be considered. The euphoria of multiple sclerosis may be brought into relation with frontal lobe lesions, but, so far as known, no demonstration of such a relationship exists.

17. Müller: Die mutiple Sklerose des Gehirns und Ruckenmarks, Jena, 1904, p. 78.

18. Hunt, J. R.: Am. J. Med. Sc. **126**:974, 1903.

increase of glia, effacement of normal cortical markings, thickening of the meninges and vascular changes, together with loss of association and tangential fibers. Clinically the case apparently does not demand a diagnosis of dementia paralytica. Multiple sclerotic lesions in various areas, including the cortex, were demonstrated. The patient's memory was defective, and there was extensive mental deterioration not incompatible with uncomplicated multiple sclerosis. That the two diseases may coexist is obvious; the differential diagnosis during life is often extremely difficult if not impossible. The recent suggestion of the relation of syphilis to multiple sclerosis is important in this connection.[19]

An illuminating case investigated by Dr. Solomon C. Fuller,[20] which he has kindly allowed me to study, is in outline as follows:

A woman, aged 47, was admitted to the Westborough State Hospital on Sept. 1, 1914, where, after three months, she died. She had contracted syphilis early in life. In 1907 she began to have difficulty in walking; the family physician thought this was caused by locomotor ataxia. She was, however, able to do her work, but with decreasing effectiveness. She became somewhat depressed and talked of suicide. Her conduct and disposition changed. Formerly neat and amiable, she became irritable and careless of her personal appearance; her memory became impaired, and speech at times was irrational. Just prior to her admission she had had several periods of excitement accompanied by violence. She created scenes on the street by using violent and profane language and showed foolish extravagance in the expenditure of money. Although unable to walk without crutches ordinarily, under the influence of excitement she was able to run with little disturbance of gait. She developed frequent incontinence of bladder and rectum. A physical examination revealed, among others, the following facts: Sense of smell was unimpaired. She insisted that she could not see well, but she was able to read a little. Movements of the eyes were unimpaired except for slight lateral oscillations (nystagmus?). The pupils were unequal; they reacted sluggishly to light and in accommodation. The fifth nerve was uninvolved except for some tremor; there was no disturbance in the facial distribution. Hearing so far as tested was not impaired; taste was unaffected; no atrophy of the tongue was present. Speech was drawling; there was elision of syllables; test phrases were poorly executed. The knee reflexes were very active. The left more so than the right. There were bilateral crossed adductor response, a bilateral Babinski sign and loss of abdominal reflexes; elbow and wrist reflexes were elicited. The finger-to-nose test was poorly executed. The Romberg test was not attempted on account of the

19. Spiller, W. G.: The Subacute Form of Multiple Sclerosis, Arch. Neurol. & Psychiat. **1**:219 (Feb.) 1919. There is also a carefully analyzed case of syphilis of the tabetic type, combined with symptoms of multiple sclerosis by Breitbach in Deutsch. Ztschr. f. Nervenh. **72**:1, 1921. Necropsy examination revealed sclerotic plaques largely confined to the dorsal tracts, together with pathologic evidence of a possibly checked syphilitic process.

20. Fuller, Solomon C.: Anatomic Findings of General Paresis and Multiple Sclerosis in the Same Case, Boston Society of Psychiatry and Neurology, Arch. Neurol. & Psychiat. **5**:757 (June) 1921.

paralysis. There was loss of bladder and rectal control; it was difficult to determine whether this was due to mental deterioration or to a focal spinal lesion.

From the foregoing history and examination the diagnosis of dementia paralytica was entirely justified and was confirmed by the necropsy examination. The evidences of multiple sclerosis during life were extremely slight. The existence of nystagmoid movements, alterations in speech, increased reflex activity and absent abdominal reflexes might have led to a suspicion of multiple sclerosis, but these symptoms were so overshadowed by the obvious paralytic dementia that they naturally were ignored. The postmortem examination revealed extensive sclerotic patches in the optic chiasm, nerves and tracts, slight lesions in the oblongata, extensive ones, particularly in the spinal cord, together with systemic dorsal degeneration of the median tract in the cervical cord and of the pyramidal tracts in the lumbar cord. The combination, therefore, on the pathologic side, of dementia paralytica, as shown by characteristic cortical as well as spinal changes, and multiple sclerosis is not to be questioned. The important etiologic question as to whether both lesions might be due to a common cause cannot here be discussed. Spirochetes could not be demonstrated. In view of the fact that there were definite sclerotic lesions, particularly in the dorsal tracts of the cord in the cervical region involving entering nerve roots, the careful examination made by Dr. Fuller is of interest from the point of view of correlation: In the upper extremities light touch sense was lost; pricks deep enough to draw blood were frequently not noted. Responses to cold and warm test tubes were in the majority of instances incorrect, and the correct responses gave the impression of happy guesses. A similar situation existed on the upper thorax. Deep pressure both here and on the arms was sometimes painful. There was loss of position sense in the fingers of the right hand; it was not disturbed in the left hand or toes, presumably on account of the position of the lesions. It would appear from this observation that all forms of sensibility are affected in a sufficiently advanced sclerotic degeneration. Whether the various types may be lost at different periods is a matter possible, but difficult, of determination.[21]

*Basal Ganglions.*—No satisfactory correlation between the lesions of the basal ganglions and the symptoms can as yet be made. The connections of these nuclei with other portions of the brain are so complex and numerous that unless the lesions are sharply limited to the ganglions, deductions of value cannot be drawn. Since this, so far as known, does not occur or has not been described, inferences only are permissible. Apparently sclerotic lesions of the striatum do

21. Breitbach: Footnote 19, second reference.

not lead to the symptoms now generally recognized as appertaining to this nucleus. The characteristic rigidities, tremors (for example, of the paralysis agitans type) and incoordinations due to lesions of this region of the brain are not conspicuous in the sclerotic syndrome. It is, however, not impossible that the ataxic tremor and alterations in tonicity may in part be due to involvement of the striatum or one of its divisions. The volitional type of motor disorder seen in Oppenheim's dystonia musculorum bears a certain distant resemblance to the gait disturbance which at times occurs in multiple sclerosis. This, however, is merely speculative, and, therefore, does not now concern us. Essentially the same may be said of the thalamus. The frequent occurrence of forced laughter and weeping, more frequent, but by no means peculiar to multiple sclerosis, finds perhaps, its best explanation in thalamic or subthalamic lesions, but obviously this location cannot be its sole cause.[22] In a recently observed patient still living so far as known, the first and for a considerable period only definite symptom was a marked unilateral astereognosis, leading to a preliminary diagnosis of brain tumor. Later typical signs of multiple sclerosis developed. The possibility of such a symptom being due to a thalamic lesion must be entertained. How far the thalamus, irrespective of its connections, may be responsible for the characteristic incoordination of multiple sclerosis must at present be left undecided so far as convincing pathologic evidence is concerned.

*Cerebellum.*—The question as to how far lesions in the cerebellum affect the symptomatology of the disease is likewise involved in somewhat hopeless confusion and again for the reason that, so far as I am aware, typical sclerotic patches limited to the cerebellum have not been described. It is a fair assumption that the cerebellum plays its part in the general disturbances of coordination, but nothing more than an assumption. If asynergia [23] is the outstanding clinical feature of cerebellar disease, we may see in the dysmetria, tremor on voluntary movement, nystagmus, speech defects, without marked alterations in sensibility, a possible correlation between cerebellar lesions and symptoms. We are, however, in no way justified in assuming that these disturbances as seen in multiple sclerosis are to be attributed only to the cerebellum and not to its connections with the brain stem and higher levels. There is danger here, as in any attempt at clear-cut localization in this disease, of overlooking various lesions in other parts of the brain in the interest of a particular area of degeneration. This is especially true in so involved an anatomic mechanism as that which underlies disturbances of motility.

22. An extreme degree of forced laughter, personally observed, occurred in a typical case of Parkinson's disease, doubtless a lesion of the striatum.

23. Tilney: Neurol. Bull. **2**:289, 1919.

*The Optic System.*—We stand on slightly firmer ground in the attempt to correlate the clinical and pathologic manifestations of the disease in the optic nerves, optic tracts and their cerebral connections, in spite of the fact that fundus changes and lesions stand in no predictable relation to each other. The basis of our knowledge in this field was laid by Uhthoff [24] in 1889 by an analysis of 100 cases with six necropsies in which the optic apparatus was particularly studied. In only one of these, no alteration was found in the nerve. In general, he found what has since been amply confirmed, that with marked pathologic changes in the nerve, the fundus may remain normal; that only slight ophthalmoscopic paling may occur, when the entire nerve is involved immediately behind the bulb; that under similar conditions often the naked nerve fibers of the papilla and others are relatively well preserved, and that there is no atrophy of the internal ganglion cell layer. It appears further that the anatomic changes, leading to disturbance of vision and alteration of fibers are due essentially to changes in the optic nerve, whereas the muscular disorders and nystagmus are dependent on central lesions naturally involving other nerves. The whole subject has been reviewed in detail by Wilbrand and Saenger.[25] Gnauck, in 1884, found sharply defined atrophy of the temporal side of the papilla and macroscopically interstitial changes in the nerves localized directly behind the bulb. Uhthoff, in 1889, pointed out the distinction between the primary atrophy of the nerve as seen, for example, in tabes, and that observed in multiple sclerosis; he also recognized the fact that under certain conditions they are not to be distinguished. Optic neuritis (a true inflammation and not due to pressure) presumably occurs oftener in multiple sclerosis than is ordinarily recognized since, owing to the character of the pathologic process, atrophy supervenes more quickly than in other conditions. Simple optic neuritis occurs in a certain proportion of all cases, 5 per cent. in 100 cases—Uhthoff, once in seventy-one cases—Frank, 13 per cent. in cases observed by Kampherstein. The occurrence of choked disk is a matter of interest. A case reported by Rosenfeld, in which there was transient choking, showed extensive lesions in the chiasm and nerve. Rosenfeld is of the opinion that sclerotic plaques directly behind the papilla may cause a true choking of the disk (Stauungspapille) which may not be regarded as an expression of general intracranial pressure since a recurrence of severe brain symptoms does not primarily lead to a repetition of the choking.[26] In general, as in other

24. Uhthoff: Untersuchungen über die bei der multiplen Herdsklerose vorkommenden Augenstörungen, Berlin, Hirschwald, 1889.

25. Wilbrand and Saenger: Die Neurologie des Auges. **5**:389, 1913. The following statements are taken largely from this review.

26. Of interest in connection with the theory that choked disk is always due to intracranial pressure (Cushing).

symptoms of the disease, these changes in the eyegrounds are likely to be transient and to give place either to recovery or slight atrophy. A rapid subsidence of swelling, apart from operation or other means for relief of pressure, is characteristic of multiple sclerosis. Apparent total or partial atrophy of the optic nerves is a much more frequent finding than choking of the disk. According to Uhthoff, ten cases, 30 per cent., showed complete atrophy ophthalmoscopically, and in 37 per cent. there was more or less marked paling of the temporal half. This condition is to be attributed to lesions in the nerve in close proximity to the papilla, but even this cannot be regarded as constant. For example, Eichhorst reports multiple sclerosis with optic atrophy in a mother and child. In both cases the cord, and not the brain, was most involved in the sclerotic process in spite of various ocular palsies and nystagmus. Oppenheim reports a case in which sclerotic changes of microscopic character were found in optic nerves and chiasm without disturbance of function. Uhthoff describes a similar case. Wilbrand and Saenger found a large, clean-cut patch of sclerosis in an optic nerve, in which the vision and ophthalmoscopic appearance were both entirely normal. The general rule applies here as elsewhere that so long as axons remain intact, function is not seriously interfered with. The varied disturbances of vision (fifty-two of seventy-one cases in Frank's statistics), sudden loss, unilateral loss, disturbance of vision as a first sign of the disease, changes in the fields, color defects, have been described by various observers.[25] A correlation between these findings and the pathologic changes in as unsatisfactory here as elsewhere. Uhthoff[27] and Lübbers[28] conclude that macroscopically a shrinkage of the nerve with extensive atrophic changes and microscopically cell proliferation and proliferative changes in general, with preponderant degeneration of the myelin, constitute the essential alterations seen in multiple sclerosis. The failure of secondary degeneration[29] due to preservation of axons accounts for the disparity between ophthalmoscopic appearances and alterations of the optic nerves. A predilection of the degenerative process for the papillomacular bundle may account for the frequent pallor of the temporal side of the disk.[30]

*Brain Stem; Other Cranial Nerves.*—The motor innervation of the eye (third, fourth and sixth nerves) is most variously affected and in the usual inconstant and erratic manner. Alterations in the size and reaction of the pupil, bilateral and unilateral, have been described in

27. Uhthoff: Untersuchungen über die bei der multiplen Herdsklerose vorkommenden Augenstörungen, pp. 408 and 442.

28. Inaugural dissertation, Marburg, 1897.

29. Buss: Deutsch. Arch. f. klin. Med. **45**:555, 1889. Description of a case with secondary degeneration.

30. Wilbrand and Saenger: Neurologie des Auges, pp. 449-452.

bewildering variety, and the Argyll Robertson pupil has been observed rarely—all without wholly adequate explanatory pathologic alterations. The same may be said of the external muscles. Spiller[31] describes a case in which an "almost complete ophthalmoplegia existed"; an area of sclerosis was found postmortem, involving the muscles of the third, fourth and sixth nerves and also the posterior longitudinal bundle. He observes, however, that the "cell bodies of the oculomotor nuclei are not very distinctly diseased." Personal cases reported in the following pages are of small assistance in clarifying the situation. In general, nothing is to be gained by a multiplication of case reports, even with detailed results of microscopic examinations, since, as repeatedly observed, no exact determination can be made of the destructiveness of the lesion by a macroscopic examination or even by a microscopic study without a very special technic. The matter is further complicated by the fact that presumably, according to Müller, who agrees with Charcot, Parinaud and Uhthoff, central rather than peripheral lesions are responsible for disturbance in ocular movements.

The crura, pons and oblongata are frequently and extensively invaded, but with relatively slight involvement of the cranial nerve innervation;[32] as for example, in a personally described case, the nuclei of all the nerves lay in sclerotic areas, with slight disorder of function (see Case 2). Oppenheim is quoted as saying that he has continually found plaques in relation to the fifth nerve, without disturbance in the sensibility of the face. On the other hand, a persistent trigeminal neuralgia was also related by him to a sclerotic patch in the nerve root.[33] Müller has never observed difficulty in mastication. The facial and hypoglossal nerves may be slightly involved; the vagus and glossopharyngeal are rarely involved. A satisfying correlation is rendered impossible here, as in the ocular innervation by the possible involvement of higher levels, cortex or conduction paths. For example, the occasionally described weakness of the facial nerves is often of the cerebral type (Müller). The nerves of special sense, other than the optic nerve, in spite of lesions involving their origins or course, are seldom affected except in minor degree.[34]

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31. Spiller, W. G.: Report of Two Cases of Multiple Sclerosis with Necropsy, Am. J. Med. Sc. vol. 125 (January) 1903.

32. Burr and McCarthy: J. Nerv. & Ment. Dis. **27**:634, 1900.

33. Nonne mentions instances of lancinating pain due to sclerotic degeneration of dorsal roots.

34. These statements are general in character. Many individual cases have been described demonstrating a somewhat definite relationship between lesion and symptom, and in many instances the various cranial nerves have been markedly involved in their function, for example, pontile and bulbar types (Oppenheim, Cassirer, Marburg and others).

*Cord.*—Owing to the small transverse area and the length of the cord, the plaques of sclerosis almost inevitably invade all the tracts as well as the ventral horns, at some level. It is not surprising, therefore, that the greatest possible multiplicity of spinal symptoms should result. Ataxia, sensory disturbance of various sorts, sphincter disorder, sex difficulties, gait disturbance, tremor, muscular weakness, hypotonicity and hypertonicity, reflex alterations, occasional muscular atrophy and in less degree vasomotor defects may occur in various combinations. To attempt a detailed correlation of these signs and symptoms with the lesions observed postmortem would lead to no profitable result. Suffice it to say that when the sclerosis is sufficiently destructive, as shown, for example, in the older areas, a simulation of any of the structural diseases of the cord may result, but even then the severity of the symptoms stands in no proper relation to the gross extent of the lesions.[35] The tendency to remissions is doubtless explained by a refunctioning of neurons, inhibited and not destroyed by the rapid development of the plaques, presumably under inflammatory conditions, much as the cranial nerves behave in epidemic encephalitis.

Interest centers particularly about the disturbances of motility in relation to predominant spastic conditions, about the relatively slight sensory defects, in spite of extensive lesions in sensory tracts, and about the rare lesions of the peripheral motor neurons sufficient to produce muscular atrophy. A tendency to spasticity is probably to be regarded as the most common sign of the disease and one of the most prolific causes of faulty diagnosis. It is usually an early sign as in my personal observation of Case 9, a case in which for a considerable period a spastic paraplegia dominated the clinical picture. More interesting and difficult of explanation are cases such as these described by Oppenheim,[36] in which after the development of a well-defined syndrome of multiple sclerosis, a spastic paraplegia later developed, confusing the diagnosis. Case 13, abstracted in the following pages, at one period so closely simulated amyotrophic lateral sclerosis that for a time the diagnosis was in doubt although earlier there had been no question of the existence of multiple sclerosis, which the necropsy confirmed.[37] Climenko [38] describes a case of spastic paraplegia with changing level in which a laminectomy was performed, with discovering the cause. The

35. André-Thomas and Comte: Rev. neurol. **14**:86, 1906. A case of paralysis of all the extremities with contractures. Necropsy revealed multiple sclerosis limited largely to the cord and particularly involving the pyramidal tracts.

36. Oppenheim: Berl. klin. Wchnschr. **33**:184, 1896.

37. Pitres: Rev. mensuelle, 1877, p. 992, describes the amyotrophic type; many have been described since.

38. Climenko: New York Neurological Society, J. Nerv. & Ment. Dis. **49**: 310, 1919.

subsequent course of the disease led him to the assumption, doubtless correct, that he was dealing with multiple sclerosis. This case bears a strong resemblance to Case 12 of my series.

Whatever the reason may be, the afferent tracts suffer much less symptomatically than the efferent corticospinal tract. General cutaneous sensibility is, as a rule, slightly affected, the sphincters more often and extensively, possibly because of the motor element in the reflex (see case reports). There are sparing descriptions of true muscular atrophy. Spiller, in the article already alluded to, speaks of atrophy as pronounced in the arms and legs, especially in the small muscles of the hand in one of his patients. A patch in a ventral horn of the lower lumbar region is pictured, and alterations of nerve cell bodies were observed. This matter is also discussed in detail by Probst,[39] but the question is not elucidated by the statement that changes in the cell bodies occurred in the upper cervical region of one case observed by him in the absence of any sclerotic focus in that region. One naturally suspects an association with an ordinary progressive muscular atrophy. In Case 13 of my series examined clinically and microscopically by Dr. Hugo Mella, the possible relation of muscular atrophy to lesions of the cervical cord with degeneration of ventral horn cells was demonstrated. It should also be borne in mind that numerous cases are on record in which symptoms simulating multiple sclerosis have been shown after death to be due to other causes, especially studied in this country by Spiller. Among these may be cited Spiller and Wood,[40] confusion with syphilis; Spiller and Camp,[41] transverse myelitis; Spiller,[42] malaria; Weisenburg and Ingham,[43] hypoplasia of the brain; Mills and Spiller,[44] arteriosclerosis; personal cases reported, Cases 6, 8, 12 and 13.

The original separation of multiple sclerosis into a spinal and a cerebral form has little to commend it because in the vast number of cases the degeneration is both cerebral and spinal. From the clinical standpoint, however, it is advisable to make certain subdivisions with the understanding that the symptoms of the various types are due predominantly to lesions in certain areas without in any sense presupposing that the lesions occur only in those areas. Marburg,[45] on the basis of the widening clinical and pathologic investigations, suggests this classification: (1) a sacral form in which the symptoms, chiefly of sphincter control, point essentially toward the lower cord; (2) a

39. Probst: Deutsch. Ztschr. f. Nervenh. **12**:447, 1898; a valuable and searching analysis of a case with correlation of symptoms and lesions.
40. Spiller and Wood: J. Nerv. & Ment. Dis. **36**:373, 1909.
41. Spiller and Camp: J. Nerv. & Ment. Dis. **31**:433, 1904.
42. Spiller: J. Nerv. & Ment. Dis. **31**:643, 1904.
43. Weisenburg and Ingham: J. Nerv. & Ment. Dis. **37**:675, 1910.
44. Mills and Spiller: J. Nerv. & Ment. Dis. **36**:747, 1909.
45. Marburg in Levandowsky: Handbuch **2**:932.

cervical form to which Cassirer has drawn particular attention; acute ataxia usually one-sided, stereognostic disturbances, slight spastic conditions and sensory disorders are characteristic; (3) a bulbar form with symptoms referring particularly to articulation, deglutition and other bulbar disturbances; (4) a pontile form involving particularly the facial and trigeminal nerves; (5) a cerebellar type characterized by asynergy; (6) a hemiplegic or hemiparetic form ushered in by apoplectiform attacks.[46] A seventh form may be added in which ocular disturbances occur early and confuse the diagnosis; and, finally, an eighth in which spastic spinal conditions, including a disorder simulating amyotrophic lateral sclerosis, are predominant. These subdivisions should not be forced too far. They evidently run into each other, and it cannot be said that the lesions in any case are limited to those portions of the central nervous system which the symptoms indicate. It is, particularly in these more focal cases, often confusing in diagnosis that a multiplicity and wide extent of the lesions often appear postmortem.

## PERSONAL OBSERVATIONS

The following cases are reported in abstract to illustrate some of the difficulties in correlation and diagnosis.

CASE 1.—Sc. Transient ocular palsies, dimness of vision, tremor of head and hands, weakness of legs, attacks of falling, incontinence, final typical picture of multiple sclerosis. Necropsy: Complete transverse lesion of lower cord with extensive degeneration of other portions, ventral and dorsal root degeneration, especially of the cauda equina, all cranial nerve nuclei in the brain stem involved; brain not examined otherwise.

In this case there was essentially complete sclerosis of the optic nerves and tracts about the chiasm, although in the clinical notes only dimness of vision is mentioned. One would also have expected more than transient ocular palsies. The tendency to fall, general weakness and incontinence, find an explanation in the extensive cord lesions completely transverse at one point, but there were less symptoms than one would have expected in so apparently complete interruption of tracts.

CASE 2.—S. Uncertainty of gait, disturbance of vision, vertigo, remission, weakness of the legs, tremor, mental failure, change in speech, pain in the legs, paresis of the legs, slight facial involvement, paresis of the external eye muscles

46. Lowrey: Am. J. Insan. **74**:395, 1918. Hemiplegia (shock) at 26, convulsions through a period of years; postmortem, gliosis of left parietal lobe, with patchy gliosis of the cord diagnosed as multiple sclerosis. Marburg: Brain Tumors and Multiple Sclerosis, a Contribution on the Localized Form of Multiple Sclerosis in the Brain, Deutsch. Ztschr. f. Nervenh. **68**: and **69**:27, 1921. Abstr. in Nelson Loose Leaf Medicine, vol. 6.

with diplopia, nystagmus, pallor of the temporal side of the disk, irregular narrowing of the fields, especially for colors, active knee reflexes, sensibility for the most part unaffected, finally paraplegia, incontinence and moderate dementia. Necropsy: Widespread lesions of the brain and cord with involvement of the cauda equina, spinal roots and cerebellar cortex, cranial nerve nuclei invaded, in general with preservation of the nerve cells; involvement of the optic chiasm and optic nerves.

The incongruity between lesions and symptoms is well shown in this case. Disturbance of vision only is mentioned although the chiasm was practically wholly invaded by sclerotic patches. Sensibility for the most part was unaffected in the presence of many lesions of the sensory tracts, especially in the cord, but also in the pons.

Case 3.—G. Examined by Oppenheim two days before death; scanning speech, probably complete bilateral external ophthalmoplegia, normal fundus, contractures, tremor of intention type, active reflexes, for six months rectal and bladder incontinence and dementia. Necropsy: Widely distributed lesions in the cord and brain, extensive cranial nerve involvement including the optic chiasm, many lesions in the capsule, centrum ovale and cerebral and cerebellar cortex.[47]

Correlations in this case are of small value because the physical examination, the report of which was available, was made so short a time before death. As given, the symptoms could not properly be accounted for by the lesions found, notably the complete external ophthalmoplegia.

Case 4.—F. N. D. Lameness and numbness of the right leg extending to the other side, improvement, articulation and vision disturbed, slight difficulty in swallowing, some ataxia, active knee reflexes, disturbance of sensation in the legs, fundus normal, again improvement; later irregularity of reflexes, crossed paralysis, spasticity, no intention tremor, nystagmus or characteristic speech defect. Necropsy: Predominating lesions of the spinal cord, nerve cells not markedly involved. This case was atypical throughout its course.

Case 5.—M. M. Emotional, sensitive to noises, speech defect, headache, staggering gait, numbness of the right hand, paresis of the right seventh nerve and of the left sixth, knee reflexes increased, nystagmus, no choking of disks, various disorders of sensibility, paralysis increasing up to death. Necropsy: Sclerotic areas throughout brain stem, no record of the cerebral hemispheres or of the cord; doubtful case during life, particularly because of well-marked sensory disturbances.

Case 6.—E. H. Active reflexes with double Babinski sign, gait weak and spastic, some numbness of the right leg, change of temperament, inequality of pupils, pain in the back and legs, muscular spasm, slow light reaction, incontinence. Necropsy: One large lesion found in the white matter of the brain and other smaller ones, numerous sclerotic areas in the cord; diagnosis of multiple sclerosis not made during life. The case suggested rather a diffuse combined degeneration of the Putnam-Dana type.

47. Cases 1, 2 and 3 reported in Deutsch. Ztschr. f. Nervenh. **5**:1, 1894.

Case 7.—E. F. Disturbed sensation in the legs, pain, difficulty in walking, knee reflexes active, double Babinski sign, some ataxia of the arms and legs, tremor of the hand, atypical scanning speech, nystagmus, increasing difficulty in walking, legs extended and spastic; no involvement of the cranial nerves, emotional, abdominal reflex absent, slight facial paralysis, speech becoming unintelligible. Necropsy: General distribution of plaques throughout the brain and cord with marked changes in the nerve roots.

Sparing sections were made from this case. So far as they are available for study the atypical character of the symptoms is somewhat adequately explained by the relative fewness of the sclerotic patches in the cord and brain.

Case 8.—C. F. R. First symptom, poor vision, staggering gait, pain, some lead found in the urine, later urinary retention, right arm weaker than the left, no objective disorder of sensation, active reflexes, cremaster and abdominal reflexes lacking, considerable unsteadiness of station, fundus normal at first examination, later suggestion of atrophy, defect of vision of the left eye; syphilis as well as lead poisoning suspected. Necropsy: Multiple sclerotic lesions. Detailed examination not made by me.

The course in this case was typical with typical lesions except that the cord appears less involved than the brain and the spastic paraplegia dominating the clinical picture for a considerable time finds no adequate explanation.

Case 9.—M. S. Weakness of the legs, temporary but recurring facial paresis, special weakness developed in the right arm and leg. For a time a spastic paraplegia dominated the picture, slight ataxia, general weakness, reflexes active, Babinski sign, slight nystagmus, speech slow and scanning, spasticity of legs without sensory disorder, increasing difficulty in walking, later extreme volitional tremor, typical scanning speech, nystagmoid movements, no continued paralysis. Pallor of temporal sides of disks, tremor of the diaphragm suggesting an intention type shortly before death. Necropsy: Cerebrospinal sclerosis, general and extensive.[48]

Case 10.—A. E. H. At 18 dragging of left foot, several falls; at 30 reeling gait with tendency to fall. Examined by J. J. Putnam and M. A. Starr. Speech defect at 37, obliged to use crutches; failing judgment, wheel chair at 43. Disease progressive with temporary improvement. For ten years unable to focus, external squint, irregularity of pupils, conversation unintelligent, mental defect well marked, no definite alteration in reflexes but tendency toward exaggeration, final difficulty in swallowing and extreme mental deterioration. Necropsy: Disseminated lesions of hemispheres, walls of the ventricles, pons and to a lesser degree in the cord.

The brain in this case was spattered with lesions, the cortex included; wherein may be found a somewhat unsatisfactory explanation of the pronounced mental changes resulting in dementia.

Case 11.—J. A. O. For six years pain in the right calf, later in the calf and ankle extending to the left side, walking became impossible, slow pupillary

48. Cases 4-9 reported in J. Nerv. & Ment. Dis. **33**:361, 1906.

reaction, no knee reflex (due probably to contractures), ankle clonus and Babinski sign present, sphincter involvement, fundus negative, Wassermann reaction negative, no mention made of tremor, nysagmus or speech defect. Diagnosis during life: transverse myelitis.

First sacral, fourth and fifth lumbar pairs of dorsal roots cut for relief of pain and with the hope of relieving the high degree of spastic paraplegia. Necropsy: Sclerotic patches were found in the crura, pons, oblongata and conspicuously in the cord. In the crura there were two small areas of degeneration. In the quadrigeminal region a well marked area in the pyramidal tract, one side; in the upper oblongata one pyramidal tract markedly involved, in the lower both pyramidal tracts. Again in the cervical cord the predominant lesions were in the pyramidal tracts, but here the sensory areas were extensively invaded as well. In the dorsal region were extensive degenerations involving both motor and sensory tracts; in the lumbar region the plaques were not so pronounced.

This case is to a certain extent but not adequately explained by the lesions. At no time was a definite diagnosis of multiple sclerosis entertained. The symptoms pointed to a fairly sharp and circumscribed transverse lesion of the cord which did not exist. The marked spasticity with tendency to contracture is doubtless explained by the definite involvement of the pyramidal tracts; the extreme pain is altogether unusual though not undescribed (Nonne), and might be explained by involvement of the dorsal nerve roots which, however, was not demonstrated microscopically. The relatively slight sensory disturbance apart from pain is noteworthy in view of the lesions found. The case in general is of rather striking interest as demonstrating the great difficulty of correct diagnosis during life.

Case 12.—C. B. Numbness and weakness of legs, girdling sensation, poor accommodation response in the left eye, tremor, absent abdominal reflex, exaggerated knee reflexes with double ankle clonus and Babinski sign, ataxia of the arms, a marked Romberg sign, spastic gait. In general, signs largely confined to the leg. Ayer double puncture, negative, colloidal gold paretic zone. Tumor of cord suspected during life; laminectomy and exposure of the cord showed various patches, presumably multiple sclerosis.

Case 13.[49]—A. C. Onset with paralysis of legs, loss of sphincter control and intense headache. Pupils unequal and irregular, right hand grasp stronger than left, knee reflexes exaggerated, double clonus and Babinski sign, Romberg sign, persistent paralysis of the leg, disturbance of pain sense, increasing incontinence, scanning speech, vertical nystagmus, slight volitional tremor, emotional, probable left astereognosis, marked muscular atrophy, especially of the left arm and hand, with conspicuous exaggeration of reflexes and spasticity of legs. Diagnosis of multiple sclerosis was repeatedly made during the earlier course of the disease; toward the end possibility of an amyotrophic lateral sclerosis was strongly entertained. Necropsy: Typical lesions of multiple sclerosis, especial interest centering in the lesions of the cervical gray matter with reference to the pronounced muscular atrophy of the hand muscles.

49. I am indebted to Dr. Hugo Mella for the clinical history and preparation of sections in this case.

Microscopic examination of the ventral horn cells in the cervical region showed certain definite changes of degenerative character though by no means so extensive as one would find in well-advanced progressive muscular atrophy of the spinal type.

CASE 14.—F. L. W. Onset with progressive weakness of the legs, associated with numbness and paresthesia, roughly up to the waist. Slight failure of vision, vertigo and tinnitus; nystagmus, both lateral and horizontal, right pupil larger than the left. Abdominal reflex bilaterally lost, loss of sense of position in legs, increasing and progressive weakness of the legs. Deep reflexes all increased but more in the legs than in the arms; ankle and patellar clonus, positive Babinski and Oppenheim response on both sides. Necropsy: Multiple sclerotic lesions of the cord with a small focus of softening in the thoracic region. The brain was not examined.

In this case the following tentative diagnoses were made during life: Tumor of the cord, combined sclerosis, transverse myelitis, and, as "a very distant possibility," multiple sclerosis. Tumor was thought to be so probable that a laminectomy was done, naturally with negative results. More importance should have been attached to the progressive weakness, the visual disturbances, the absent abdominal reflexes and to the colloidal gold reaction which was in the syphilitic zone in the absence of all other findings in the fluid suggestive of syphilis.

This group of cases illustrates in concrete form the difficulties of diagnosis and the impossibility of accurately correlating the clinical symptoms with postmortem findings. A cursory analysis emphasizes these points: A definite antemortem diagnosis was consistently made in only six cases, and one of these was doubtful during the latter part of life. The lesions stood in no predictable relation to the signs and symptoms during life, notably those of the oblongata and pons involving the cranial nerves. Several of the cases with generally disseminated lesions, strongly suggested sharply localized defects, for example, Case 11, transverse myelitis, Cases 12 and 14, tumor of the cord, Case 13, in late stages, amyotrophic lateral sclerosis. This is wholly in accord with the observations of many others and requires no further comment. It is evident that exact correlations cannot be made.

## CONCLUSIONS

In summarizing this involved question the following conclusions appear to be warranted by the facts as yet at our disposal: As in other structural diseases of the nervous system, a general correlation may be made between lesions in certain localities and symptoms due to such lesions. It rarely happens that symptoms occur without any discoverable lesion. The degree of disturbed function depends on the age of the lesion, since the older the lesion the greater the destruction of nerve elements. The most satisfactory correlations have been made in connection with vision and the optic nerves and tracts. Sensory, motor or mental disorder may certainly be attributed to lesions

occurring in the areas of the central nervous system disturbing these functions; but a precise determination of lesions from symptoms or of symptoms from lesions is not possible on account of the peculiar type of degeneration in the disease, particularly the long persistence of axons, the resistance of cells, and the multiplicity of lesions, which confuses the clinical picture. For instance, one is not justified in attributing mental changes to lesions of the cortex, when association tracts and deeper structures are also involved, nor can we say that ocular or other palsies are due to nuclear lesions when the cortical controlling areas or the connecting pathways are likewise involved. A wholly satisfying explanation of the so-called cardinal symptoms of the disease is not yet forthcoming. It is, however, fair to assume that the loss of myelin and the localization of lesions in coordinating areas are both, in part, responsible for the characteristic volitional tremor in its manifestation as nystagmus, speech defect and general ataxic tremor. Apart from these somewhat unique disturbances, the other signs and symptoms of the disease which are coextensive with the symptomatology of the nervous system in general, find their explanation in the multiplicity of the lesions, their localization and their degree of destructiveness. An attempt to draw accurate physiologic deductions is usually fallacious, and always misleading.

# INCIDENCE OF MULTIPLE SCLEROSIS IN UNITED STATES TROOPS

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During the recent mobilization the neuropsychiatric officers examined approximately 3,500,000 men, draftees and volunteers. The examinations were made at the camps, and in the case of draftees, after acceptance by draft boards.

A total of 69,394 cases of nervous and mental disease and defects were identified. They were divided into nine clinical groups. The subhead under which multiple sclerosis was classified was entitled "Organic Diseases and Injuries." It included injuries, the general organic diseases of the nervous system, syphilis of the central nervous system (exclusive of paresis), a few minor conditions, such as tics, myasthenias, myotonias and other conditions. This group embraced 6,916 cases, about one-tenth of the total number.

Our method of approach to a determination of the frequency of multiple sclerosis is to determine its frequency, not in relation to the number of men examined, but in relation to other nervous conditions found in the particular group to which it belongs. For example, among 6,916 so-called organic cases, there were 511 cases of multiple sclerosis. We may say, therefore, that multiple sclerosis has a distribution average among organic conditions of 7.4 per cent.

Variations from this average occurred in certain states and in certain races. The variations in states was in approximate agreement with the results given in "Defects Found in Drafted Men." The variations as to races are given in the table.

Of the fractions given in the table, the numerator indicates the number of cases of multiple sclerosis found in the race, and the denominator indicates the total number of cases of general organic conditions in that race. The resulting percentage is the percentage of cases of multiple sclerosis as compared to organic conditions in that race. It will be observed that the percentage of cases of the disease in the Scandinavians, the French, the Slavs, the Scotch, the Germans, the English and the Irish all exceed the general distribution rate of multiple sclerosis. Also, there was an excess of cases in the foreign-born as compared with the native-born.

The average of foreign-born in the whole group of organic conditions was 9.2 per cent., while in multiple sclerosis it was higher, namely, 12.7 per cent. Thirty per cent. of the patients with multiple

sclerosis gave a family history of nervous diseases (as compared with syphilis of the central nervous system, for example, in which only 7 per cent. of the patients had a family history of nervous diseases); 10 per cent. gave a family history of mental disease.

PERCENTAGE DISTRIBUTION OF MULTIPLE SCLEROSIS AMONG INJURIES AND DISEASES OF THE NERVOUS SYSTEM AS DETERMINED IN CERTAIN CLASSIFIED RACES

Total number of cases of nervous diseases and injuries..6,919
Total number of cases of multiple sclerosis..... 511

Average distribution rate of multiple sclerosis.....7.4%

| | Cases of Multiple Sclerosis | Cases of General Organic Diseases | Percentage |
|---|---|---|---|
| African | 28 | 800 | 3.5 |
| Dutch | 4 | 38 | 1.0 |
| English | 74 | 913 | 8.1 |
| French | 11 | 102 | 10.7 |
| German | 35 | 418 | 8.3 |
| Irish | 41 | 516 | 7.9 |
| Italian | 10 | 191 | 5.2 |
| Scotch | 8 | 96 | 8.2 |
| Scandinavian | 16 | 127 | 12.5 |
| Slav | 18 | 181 | 9.0 |

# LESIONS OF THE AUDITORY AND VESTIBULAR APPARATUS IN MULTIPLE SCLEROSIS

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These clinical studies of auditory and vestibular signs in multiple sclerosis are based on the examination of ten cases in which the diagnosis of this disease had been made. The examination divides itself naturally into: (1) a determination of the status of the sense of hearing; (2) the estimation of the presence or absence of spontaneous signs of disturbances in the vestibular apparatus, and (3) the observation of the character of the responses to experimental vestibular stimulation.

All ten subjects of this examination had normal middle ears. In none was there any disturbance of hearing, and there was no history of deafness. Transitory deafness, however, does occur as a symptom of multiple sclerosis, and has been reported by Beck [1] in two cases. In a third case, in which the diagnosis was not positive, there were temporary disturbances in hearing, of the nerve type. He believes this analogous to the transitory amaurosis, which occurs in multiple sclerosis. Hess,[2] Oppenheim [3] and Marburg [4] have also observed transitory deafness. Bárány [5] has reported a case of multiple sclerosis in which the diagnosis originally was acousticus tumor. This patient was operated on, and the tumor was not found. Subsequent to the operation, Bárány reexamined him, and found unilateral total deafness, with loss of nystagmus, following experimental vestibular stimulation, but with normal vertigo and past pointing. The original diagnosis of acousticus tumor was based on the erroneous assumption that the eighth nerve had undergone complete loss of function. The second examination showed the astounding peculiarity that, although nystagmus did not appear as the result of caloric labyrinthian stimulation, vertigo and past pointing did. Bárány concludes from this observation that the lesion could not involve the eighth nerve itself, but must be located in the brain stem beyond the point at which the vestibular fibers have separated into their tracts.

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1. Beck, O.: Gehörorgan und multiple sklerose, Monatschr. f. Ohrenh. **47**: 875-877, 1913.
2. Hess: Arch. f. Psychiat. **19**:1888.
3. Oppenheim: Berlin klin. Wchnschr. 1896, p. 185.
4. Marburg: Die sogenannte akute multiple Sklerose, Leipzig and Vienna: Deuticke, 1906.
5. Bárány: Zur Differentialdiagnose zwischen Acusticustumer und multipler Sklerose mit bulbärem Sitz, Monatschr. f. Ohrenh. **47**:693-694, 1913.

### NYSTAGMUS

With regard to the spontaneous signs of disturbances in the vestibular apparatus, the most important, perhaps, is nystagmus. This occurred in seven of the ten patients examined. Nystagmus was recognized by the older neurologists as a cardinal symptom of multiple sclerosis, and is considered an important one by modern neurologists. It occurs in a little over 50 per cent. of the cases. In the patients examined by me, spontaneous nystagmus occurred in all directions, that is, to both sides, upward, downward and obliquely. In some cases, several of these were combined. The spontaneous nystagmus, too, varies in type. As a rule, the lateral or horizontal nystagmus predominates. In one instance, there was a combination of rotary and horizontal nystagmus. The nystagmus is of two varieties: (1) oscillations of the eyeball, and (2) definitely rhythmic movements. A vertical nystagmus upward or downward occurred in four of the ten cases. This is considered pathognomonic of a lesion in the brain stem. One of the striking peculiarities regarding the spontaneous nystagmus is that it frequently persists despite the superimposed induced nystagmus, so that in response to cold caloric stimulation one may have a normal nystagmus directed to the side opposite to the ear which is stimulated, and yet the spontaneous nystagmus in some other directions will persist, and may even be accentuated. Occasionally it seems as if the spontaneous and induced nystagmus combine and cause most bizarre ocular movements. Another striking peculiarity in the patients examined was the loss of conjugate movements of the eyes, following induced nystagmus. Thus, in four instances, as the result of caloric stimulation, both eyes executed nystagmic movements, normal in their direction and plane, but differing in rhythm in the two eyes. Manifestly, the integrity of the mechanism that controls conjugate eye movements is essential to the normal play of induced vestibular nystagmus. In four of the ten cases, caloric stimulation caused a skew deviation, which did not occur spontaneously. In several instances, caloric stimulation was unable to produce definite responses. In one case, caloric stimulation of one set of vertical canals did not cause nystagmus, but did arouse normal vertigo and normal past pointing.

### VERTIGO

Leidler[6] says that vertigo is a common symptom of multiple sclerosis. In none of the cases observed, however, was there at the time of examination any evidence of vertigo, as determined by the pointing tests. None of the ten patients showed spontaneous past pointing. In several of the cases, because of the tremendous intention

6. Leidler, R.: Ueber die Beziehungen der multiplen Sklerose zum zentrale Vestibular-Apparat, Monatschr. f. Ohrenh. **51**: No. 56.

tremor, pointing tests were impossible; but where they were made, the general direction of the arm movement was conserved, the tremor interfering only with the nice approximation of finger to finger. In no instance have I observed the hyperirritability described by Bárány. In fact, it has seemed to me that even when nystagmus following caloric stimulation approximated normal, vertigo was frequently suppressed, and nausea and vomiting never occurred.

### REPORT OF CASES

Case 1.—A. B., 41 years of age, had been ill for six years. Examination revealed: middle ears and tone limits normal; in the Weber test a vibrating tuning fork placed on the vertex was heard in the head, that is, not referred to either ear; Rinné's test, both sides, positive; Schwabach test normal; spontaneous nystagmus directed in both sides, more marked toward the right, also directed upward; no vertigo; no past pointing with either arm; rotation to the right after nystagmus of good amplitude, to the left, forty seconds; rotation to the left after nystagmus of good amplitude, to the right, thirty-five seconds; turning to the right, normal past pointing to the right, both arms; turning to the left, normal past pointing to the left, both arms; caloric test of the right vertical canals, feeble nystagmus, with normal past pointing; caloric test of the right horizontal canal, normal nystagmus, with normal past pointing. Caloric test of the left vertical canals caused no rotatory nystagmus to the right, but an increase in the spontaneous vertical nystagmus upward, with, however, normal past pointing to the left. Caloric test of the left horizontal canal gave a normal response.

Case 2.—W. F., 60 years of age, had been ill for thirty years. Examination revealed: middle ears and tone limits normal; no spontaneous nystagmus or past pointing; caloric stimulation of the left vertical and left horizontal canals aroused no nystagmus, but both arms past pointed 6 inches (15.24 cm.) to the left. This case was analogous to that described by Bárány, with the exception that hearing was normal. Caloric stimulation of the right vertical and horizontal canals gave normal responses.

Case 3.—J. C., 43 years of age, had been ill for six years. Examination revealed: both middle ears and tone limits normal; spontaneous horizontal nystagmus to the right and upward, none to the left; no vertigo or past pointing. Caloric stimulation of the left vertical canals was positive. There was normal vertigo with normal past pointing. Nystagmus following stimulation was of a peculiar dissociated type. Skew deviation also occurred, as well as an increase in the spontaneous nystagmus upward. Stimulation of the right side was normal.

Case 4.—O. H., 49 years of age, had been ill for nineteen years. Examination revealed: normal middle ears and tone limits; spontaneous, irregular, oblique nystagmus to the left; a combined rotatory and horizontal nystagmus to the right; an upward and a downward nystagmus. Pointing tests were impossible because of intention tremor. Caloric stimulation of the right vertical canals caused a definite increase in the spontaneous nystagmus to the left, but did not abolish the nystagmus upward or that to the right. Here, too, there were peculiar dissociated eye movements, resulting from caloric stimulation, and at times a skew deviation.

CASE 5.—J. S., 51 years of age, had been ill for fifteen years. Examination revealed: normal middle ears and tone limits; despite considerable intention tremor, normal pointing; a peculiar spontaneous dissociated nystagmus, more marked in the eye of the side toward which the eyes were directed, also a vertical nystagmus upward. Caloric reaction of the right vertical and horizontal canals was positive, resulting in a peculiar dissociated nystagmus and skew deviation, but arousing no vertigo or past pointing. Caloric test of the left vertical and horizontal canals aroused a similar response.

CASE 6.—A. S., 30 years of age, had been ill for seven years. At present he is bed-ridden. Examination revealed: normal middle ears and tone limits; Rinné's test, both sides, positive; Schwabach test normal; spontaneous nystagmus directed to both sides and upward; pointing test in the left arm impossible, in the right arm despite tremendous tremor, the direction of the movement was conserved, and although the arm oscillated somewhat, finger touched finger accurately. Caloric test of the left horizontal canal (impossible to sit up, therefore, vertical canals were not tested) caused marked response with slow nystagmus directed to the right; at times there was a skew deviation. There was no vertigo and no past pointing. Caloric test of the right external canal aroused a similar response and occasioned dissociated eye movements and slow nystagmus. There was no vertigo or past pointing.

CASE 7.—F. I. K., 55 years of age, had been ill for thirty years. Examination revealed: normal middle ears and tone limits; no spontaneous nystagmus and no spontaneous past pointing. The caloric test of the left vertical canal aroused a tardy, feeble response; in the left external canal it aroused a more nearly normal response. On the right side the results were similar, but neither labyrinth aroused vertigo or past pointing.

CASE 8.—A. M. W., 35 years of age, had been ill for seven years. Examination revealed: normal middle ears and tone limits; spontaneous lateral nystagmus directed to both sides; on looking upward, an oscillatory lateral movement in both eyes, much more marked in the right; no vertical nystagmus; no vertigo or spontaneous past pointing. Caloric stimulation of the left external canal aroused a horizontal nystagmus to the right, with normal vertigo and past pointing. Caloric stimulation of the right vertical and horizontal canals gave normal responses, with the exception of the asynchronous character of the nystagmus.

CASE 9.—L. F., 37 years of age, had been ill for three years. Examination revealed: normal middle ears and tone limits; coarse, nystagmic movements directed to both sides, chiefly right, none upward or downward. The pointing was fairly accurate, the direction being conserved, the tremor interfering only with the accurate contact with the finger. Caloric stimulation of the left vertical and horizontal canals gave normal responses. The vertigo, however, and the past pointing were slight. Caloric stimulation of the left labyrinth gave similar responses. The nystagmus resulting from caloric stimulation differed from the nystagmus in normal persons in that it was slower, more like a nystagmus of central origin.

CASE 10.—In I. C. both middle ears and tone limits were normal. Rinné's test was positive, the Schwabach test normal. There was no spontaneous nystagmus, no vertigo, no past pointing. Caloric stimulation of the right vertical canals and right horizontal canal aroused normal responses. Caloric stimulation of the left vertical and horizontal canals also aroused normal responses.

COMMENT

It would be exceedingly rash to dignify a discussion of the clinical data here presented by the term "conclusion," so much still rests on speculation and so little on definite knowledge. From these examinations, however, there have sprung certain suggestions which are at least worthy of mention:

1. The usual type of spontaneous nystagmus (namely, rhythmic), combined with the fact that it is frequently not amenable to influences aroused by vestibular stimulation, suggests that the origin of the nystagmus is a lesion in the vestibulo-ocular mechanism.

2. It is certain that as the result of vestibular stimulation, nystagmus and vertigo and past pointing may at times be aroused independent of each other. This may be true not only of the static labyrinth as a whole, but may apply also to the individual canals, at least to the vertical canals, as differentiated from the horizontal. These facts suggest a difference in location between the vestibular nuclei or tracts which intermediate nystagmus impulses and those which have to do with the sense of position in space.

3. It appears, further, from Beck's cases, that nystagmus, vertigo and past pointing may be aroused by experimental vestibular stimulation, and yet the falling cannot be influenced by changes in the position of the head. This fact suggests a difference in the location of the vestibular nuclei or tracts that intermediate so-called vertigo impulses to the extremities and those which transmit similar impulses to the trunk.

4. The presence of induced nystagmus with the total loss or marked suppression of vertigo, as seen in Cases 5, 6, 7 and 9, suggests the possibility of extensive disease of the cerebellar nuclei, or of the cerebellocerebral tracts, as the cause of this phenomenon.

5. Finally, it is clear that careful clinical study, combined with histologic research in cases of multiple sclerosis, will do much to clear up the shadows still overhanging an understanding of the anatomy and physiology of the central portion of the vestibular apparatus.

# STUDIES IN THE PATHOGENESIS OF MULTIPLE SCLEROSIS *

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This article contains a brief review of the histopathologic changes in multiple sclerosis studied on material from thirteen cases. Two cases came from the neurologic service of Cook County Hospital; for two I am indebted to Dr. Peter Bassoe of Chicago; for one to Dr. Theophil Klingman of Ann Arbor, Michigan, and for eight to Dr. Alfons Jacob of Hamburg, Germany.

In addition, four other cases were studied; two apparently normal cords, one cord from a case of capsular hemiplegia and one from a case of Recklinghausen's disease. The findings were contrasted.

The best known and the most notable characteristic features of multiple sclerosis are the so-called patches of sclerosis. Scattered throughout the central nervous system and varying in size and form they preferably affect the white substance, its long or short nerve fibers; they may be symmetrical or asymmetrical and may invade even the peripheral nerves (Strahüber,[1] Schob[2]). Wherever located, whatever the size or age (young or old), there can be discerned in a patch many nerve fibers in fairly good condition. A great many are merely deprived of myelin, appearing as naked axons (demyelinated nerve fibers); some are partially covered with myelin, while others show a destruction of both the myelin and axon, exhibiting a state of wallerian degeneration.

These three pathologic features—apparently healthy fibers, fibers totally or partially demyelinated and fibers in a state of wallerian or secondary degeneration—occur not only in the patches themselves but also in parts of the central nervous system which show no visible

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* From the laboratories of the Illinois State Psychopathic Institute and Cook County Hospital.

* Presented before the second annual meeting of the Association for Research in Nervous and Mental Diseases, New York, Dec. 28-29, 1921.

1. Strahüber, A.: Ueber Degenerations-und-Proliferationsvorgänge bei multipler Sklerose des Nervensystems, Ziegler's Beitr. z. path. Anat. **33**:409, 1903. Bemerkungen zu der Arbeit des Herrn Bielschowsky: Zur Histologie der multiplen Sklerose, Neurol. Centralbl. **23**:55, 1904.

2. Schob, F.: Ein Beitrag zur pathologischen Anatomie der multiplen Sklerose, Monatschr. f. Psychiat. u. Neurol. **22**:62, 1907.

patches. Even an ordinary stain, that of Weigert-Pal for instance, brings out some of these features. Thus Figure 1 shows distinctly an old patch involving the posterior columns of the spinal cord where it appears as a pale island. On closer examination, with a hand lens or a microscope, one can discern in the colorless island a number of well preserved fibers in the shape of black dots. These represent a transverse section of normal nerve fibers separated from each other by empty spaces.

Between the pale patch and the normal-looking lateral columns there is an area containing a much greater number of nerve fibers of normal appearance. Such an area, termed intermediate, transition, adjacent or superimposed, is generally looked on as a young, undeveloped patch, the further growth of which has been prevented by death. An

Fig. 1.—Eighth thoracic segment; patches in the posterior columns, the right lateral column and in the right posterior horn. The transition zone in the posterior columns, between the patch and the normal looking remnants of Burdach's columns, is marked. Weigert-Pal stain; × 13.

ordinary stain conveys the impression that an old patch grows by a gradual spreading in width, not respecting the neighboring tissues, the glia, blood vessels or the septums. It is also assumed that small plaques, gradually increasing in size, become coalescent to form a larger focus which sometimes may cover the entire width of the spinal cord.

A much better idea as to the origin of a plaque, its growth and its relationship to the neighboring structures may be gathered from specimens stained with the methods of Marchi, Bielschowsky, Mallory-Jacob, Alzheimer-Mann, and especially with the combined staining methods of Marchi-Alzheimer-Mann or Bielschowsky-Alzheimer. The latter method

brings out with remarkable clearness the various healthy and pathologic structures.[3]

Figure 2, a photomicrograph of a longitudinal section of an apparently healthy area stained with Bielschowsky and counterstained with the method of Alzheimer-Mann, shows very well the axons, the


Fig. 2.—Longitudinal section of normal looking remnants of Burdach's columns. The black irregular lines are axons; the surrounding myelin either is swollen or shows minute globules (Elzholz bodies). Many of the black globules are parts of the axons which had been irregularly cut. In the center a myeloclast is seen within a large vacuole, *Mcl.* Use a hand lens. Bielschowsky-Alzheimer-Mann stain; × 560.

myelin and the glia. The axons show no particular changes, but the myelin sheath is tumefied, forming a broad swollen band around the well preserved axons. In many places the myelin appears fragmented,

3. This combination stain has been described by me in "A Contribution to the Histogenesis of Syringomyelia," ARCHIVES OF NEUROLOGY AND PSYCHIATRY **3**:130 (Feb.) 1920. In brief it is as follows: Bielschowsky sections not impregnated with gold are placed in a solution of phosphomolybdic acid (about 30 to 60 minutes), then in Mann's mixture (a 1 per cent. solution of methyl-blue eosin); differentiate in 95 per cent. and absolute alcohol.

broken up into globules and droplets. Under the oil immersion there can be observed in the myelin more or less wide meshes giving the myelin a reticulated or fenestrated appearance, as if it consists of numerous holes through which the axon can be distinctly seen. The distended meshwork of the myelin sheath frequently breaks down resulting in the formation of cavities, so-called "Lücken" (Fig. 3).

Marchi stained specimens, especially when counterstained with Alzheimer-Mann's or Mallory-Jacob's methods, exhibit, in addition to the marked swelling and fenestration of the myelin, numerous small

Fig. 3.—Longitudinal section of a "normal area." *A*, axon; *M*, myelin; broken up into globules (Marchi globules); *L,L*, "Lücken" crossed by an axon. The tissues between the axons are glia fibers and glia nuclei (dark round bodies). Bielschowsky-Alzheimer-Mann stain; × 450.

black structureless droplets (Elzholz bodies) scattered along the axon and intermingled with fragments of broken up myelin. The myelin fragments may be of smaller or larger size, are made up of concentric layers, stained dark brown or black with osmic acid and are known as Marchi globules (Fig. 3 *M*).

The outlined changes—swollen fenestrated myelin, its fragmentation with abundant formation of Elzholz bodies and Marchi globules

in the presence of a well preserved axon—were found, in all of the thirteen cases studied, outside the patch proper, in areas which, with ordinary stains, appeared normal. The changes are exactly similar to those described as periaxial neuritis by Gombault,[4] Stransky [5] and especially well by Doinikow [6] in experimental degeneration of peripheral nerves. It would therefore be logical to assume that the earliest changes of multiple sclerosis obtained in the myelin are in the nature of periaxial neuritis.

The myelin changes, however mild, were always accompanied by marked proliferative phenomena in the glia tissue. The latter showed either as an increased amount of glia fibers filling up the spaces between

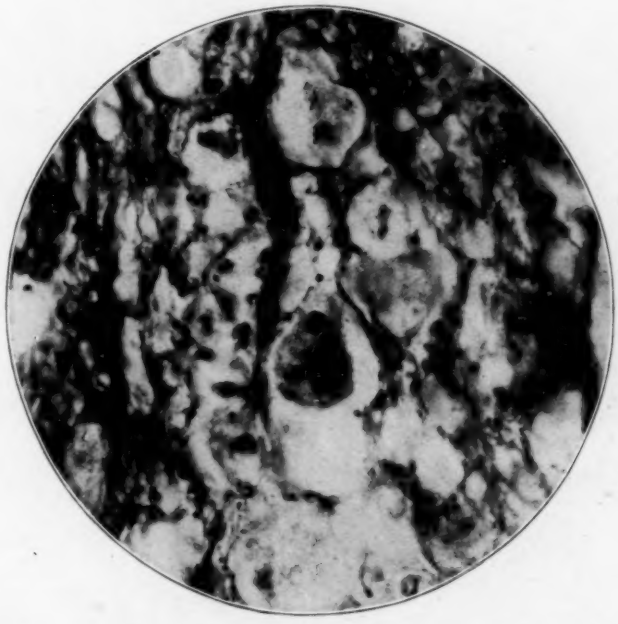

Fig. 4.—A group of myelophages. The one in the center of a large vacuole contains within one of its own vacuoles an amyloid body (use a hand lens). Mallory-Jacob stain; × 560.

the parallel running, swollen nerve fibers, or as large glia nuclei, rich in chromatin, invested by a visible, well-developed membrane and abundantly supplied with cytoplasm. The glia cells often appeared as

4. Gombault, M.: Contribution à l'étude anatomique de la nevrite parenchymateuse subague et chronique. Nevrite segmentaire periaxile, Arch. de neurol., 1880-1881, vol. 1.

5. Stransky, E.: Ueber diskontinuierliche Zerfallsprozesse an den peripheren Nervenfasern, J. f. Psychol. u. Neurologie **1**:169, 1903.

6. Doinikow, B.: Beiträge zur Histologie und Histopathologie des peripheren Nerven, Nissl-Alzheimer's Arb. **4**:445, 1911.

large astrocytes (Deiters' cells) with numerous branching processes, breaking up into thin fibrils. Other glia cells, again, appeared greatly changed. They were lying within vacuoles, and presented large, somewhat broken-up granular cell bodies with an eccentric pyknotic nucleus and contained within their cytoplasm minute droplets of lipoids. These gliagenous formations are myeloclasts (Fig. 2, *Mcl*) described by Jacob [7] in the earliest stages of secondary degeneration of the central nerve fibers.


Fig. 5.—Transition zone, longitudinal section. The axons, *A,A,* are fewer though well preserved. Many "Lücken" show fragments of myelin, *M,M; G* indicates the space occupied by gitter cells, α and γ varieties; the black bodies are nuclei of gitter and other glia cells. Bielschowsky-Alzheimer-Mann stain; × 300.

Equally marked were mesodermogenic changes in the blood vessels, pia and its septal prolongations. They all exhibited a pronounced hyperplasia and thickening, dilatation of the perivascular adventitial

7. Jacob, A.: Ueber die feinere Histologie der sekundären Faserdegeneration in der weissen Substanz des Rückenmarks, Nissl-Alzheimer's Arb. **5**:1, 1912. Experimentelle Untersuchungen über die traumatischen Schaedigungen des Zentralnervensystems, Ibid., pp. 182-333.

spaces which were packed with gitter cells and distention of the pial meshes.

CHANGES IN THE INTERMEDIARY ZONE

Much more in evidence were the ectodermogenic (nerves and glia) changes in the intermediate area, or, where this was not well formed, in the regions adjacent to the plaque proper. The Marchi globules which began forming in the "healthy" areas were here more numerous. The axons were usually well preserved; sometimes they were slightly

Fig. 6.—Vessels infiltrated with gitter cells. The entire field is covered with fat laden gitter cells appearing as so-called "fat granule myelitis." Herxheimer scarlet red stain; × 60.

tumefied, finely granular, twisted and occasionally broken up into minute fragments. Both the myelin (or Marchi) globules and the fragments of the axons were enveloped by glia rings or were enclosed within gliogenous cell bodies containing larger or smaller vacuoles and an eccentric chromatin-rich nucleus. These are Jacob's myelophages (Fig. 4) which, according to this investigator, pick up the broken-up nerve tissue and transform it within their vacuoles into fatlike (lipoid) substances.

These lipoids are found in larger masses within a third type of gliogenous formations, generally known as gitter cells or fat granule bodies (Fig. 5). The latter, as well as the myelophages, denote a further, more advanced, stage of secondary nerve degeneration than the stage of Marchi globules and myeloclasts.

The gitter cells generally appear as fine reticular honey-combed bodies harboring within their delicate vacuoles the lipoids resulting from the digestive activities of the myeloclasts and myelophages. In

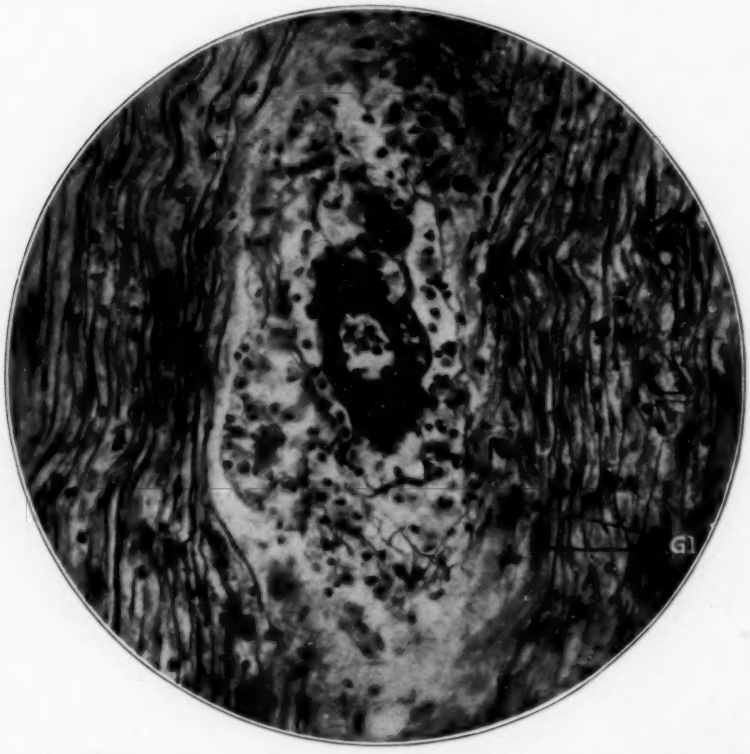


Fig. 7.—Blood vessel with a dilated adventitial space (Virchow-Robin) packed with gitter cells. The surrounding axons are well formed; *Gl*, protoplasmic glia cells which are very numerous here. Bielschowsky stain; ×260.

human pathologic material it is possible to follow up the transitions from a myelophage to a gitter cell which thus most probably represents a further evolutional stage of myelophage. Jacob [7] holds that the gitter cells, like the myeloclasts, undergo regressive changes, after the process of transformation of the broken-up myelin and axon is accomplished. Many gitter cells still show a large vacuole with remnants of nerve tissue within (gitter cell $\alpha$), some show large vacuoles packed with large globules of lipoids (gitter cells $\beta$) and some show only minute vacuoles filled with very small droplets of fat. The cells

of the last variety are round and appear freely scattered over the field of vision as well as in large masses around the vessels or between the glia fibers and even in the pia (gitter cells $\gamma$).

The presence of vast numbers of various fat laden gitter cells gives the field of vision a characteristic appearance (especially when stained with osmic acid, scarlet red [Fig. 5] and similar strains) described by some authors (Dawson,[8] Klingman[9]) as the stage of fat granule myelitis. In general, such an area in no way differs from that resulting

Fig. 8.—Cortex; swollen myelin fibers; the lower nerve fiber shows fenestration and swelling; others are bulb shaped, spindle shaped or varicose. Frozen section stained with Weigert-Pal; × 300.

from secondary degeneration, for instance, of the lateral spinal cord columns following internal capsular destruction.

The vessels in the intermediate area are more numerous but show the features outlined in the foregoing—the walls are thickened but

8. Dawson, J. W.: The Histology of Disseminated Sclerosis, Proc. Royal Soc. of Edinburgh **50**: 1914; Rev. neurol. & Psychiat. **15**:47, 367, 1915; **16**:287, 1916; Edinburgh M. J., N. S. **17**:229, 311, 377, 1916.

9. Klingman, T.: The Histogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **1**:39, 193 (Jan., Feb.) 1919.

usually dilated (Fig. 7), the dilated spaces containing an enormous number of gitter cells (γ variety). In toluidin blue, thionin, hematoxylin-eosin, van Gieson and similar stains such infiltrated blood vessels suggest at first glance an inflammatory condition, as if the infiltration consists of lymphocytes, plasma cells and similar hematogenous elements. Such an error can easily be corrected by having the specimens stained with osmic acid or scarlet red which will show that the infiltrating cells are fat granule bodies (gitter cells). The latter are the principal constituents of the infiltrated adventitial spaces;

Fig. 9.—Patch of sclerosis represented by a glia tissue scar. The undulating lines are glia fibers covered with numerous glia nuclei. Vessels are few; axons present but few. Bielschowsky-Alzheimer-Mann stain; × 140.

lymphocytes, polyblasts and plasma cells were exceptionally rare, and only in the brain substance, not in the cord, and even when present were greatly changed and degenerated. Polymorphonuclear elements did not show at all.

Some blood vessels or capillaries were devoid of infiltration; the adventitial spaces were not dilated but on the contrary collapsed and thickened, often exhibiting numerous nuclei; the lumen, as a rule, was unobstructed, the endothelium very prominent.

The great number of blood vessels infiltrated with gitter cells or possessing thickened walls is another characteristic feature of the transition zone. Yet even here one may find numerous Marchi globules, many nerve fibers, swollen and reticulated (Fig. 8) and even nerve fibers in a fairly good condition. In short, the transition zone is made up of nerve fibers in various stages of degeneration, in no way differing from changes described by Jacob in secondary degeneration.

It is only proper to point out that a transition zone is often lacking, that is to say, a patch frequently ends abruptly without shading off

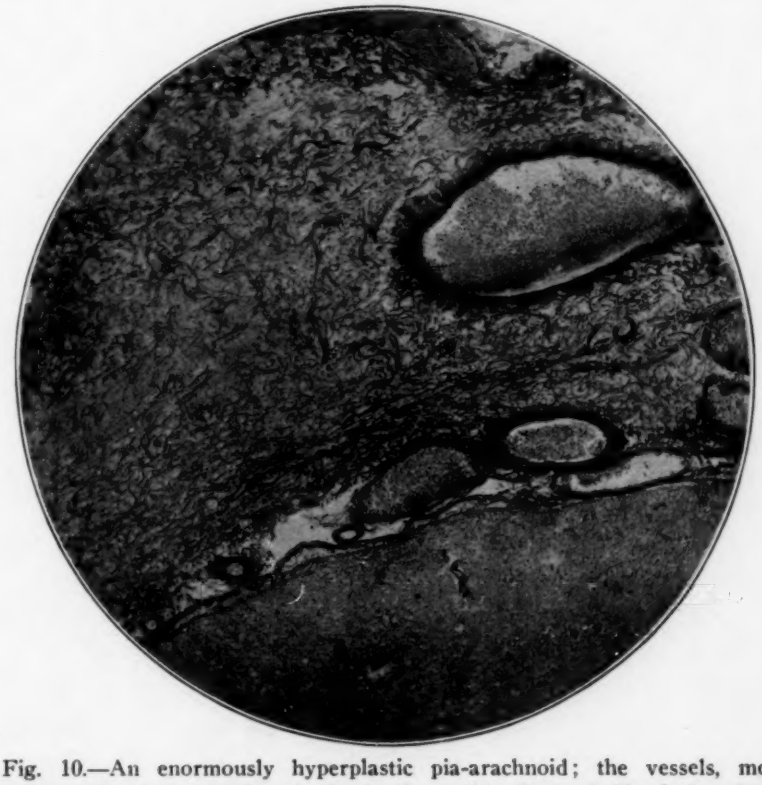

Fig. 10.—An enormously hyperplastic pia-arachnoid; the vessels, mostly veins, are also hyperplastic; the brain tissue (the lower half of the picture) shows distinct small vessels with thickened, not infiltrated, walls. With the help of a hand lens, many infiltration cells can be seen in the meshes of the pia-arachnoid as well as other changes. Alzheimer-Mann stain; ×60.

into an apparently normal area. Yet, even in such instances there can be found, in the vicinity of the patch, nerve fibers in a state of advanced degeneration as outlined in the foregoing (Fig. 8).

### PATCH OF SCLEROSIS

After the broken up fragments of myelin and axons have been transformed by the action of the myeloclasts, myelophages and gitter

cells into lipoids and removed to the mesodermogenic tissues—blood vessels and the pia-arachnoid, in other words, after the damaged tissues have been cleaned up and freed of the scattered débris, the destroyed nerve tissue is replaced by a so-called glia tissue scar, a patch of sclerosis (Fig. 9). In its typical form it consists of very thin neuroglia fibrils emanating from richly stained oval or rodlike nuclei, and so thickly packed that hardly any interspaces can be discerned. In other instances, there is an abundance of cytoplasmic glia cells, homogeneous in appearance, possessing an eccentric chromatin-rich anucleus and a great mass

Fig. 11.—Optic chiasm covered with thickened hyperplastic vessels and pial septums. Mallory-Jacob stain; × 10.

of thin processes. Again, there are instances in which the glia scar does show interspaces. The size of any interspace is very small, one gitter cell being sufficient to fill it up. Scarlet red stain shows, in a glia scar, an abundance of minute, dustlike droplets of lipoids enclosed either within the glia nuclei and gitter cells or scattered over its surface.

Notwithstanding such severe destruction, a stray nerve fiber covered with myelin may be encountered even in such deserted areas. More

commonly, however, the scar tissue exhibits nerve fibers deprived of myelin, that is to say, nerve fibers represented by naked axons, running wavelike and parallel to the glial fibrils. They usually appear thinned, granular, distinctly fibrillar and often are difficult to differentiate from the glia. New formed or regenerated axons, as described by Popoff,[10] Strahüber,[1] Doinikow [11] and others, could nowhere be found. Blood vessels in the scar tissue are less conspicuous than in the intermediary area. They often show masses of lipoids within the adventitia, which is usually thickened. Inflammatory phenomena, as in previous stages, were absent.

The scar patch is thus to be considered the final stage of nerve degeneration which began as swelling and fragmentation of the myelin (Marchi-globule stage), continued as a stage of myelophage and gitter cell activity and ultimately resulted in the formation of a glia scar. The three consecutive stages of a patch evolution [12] in multiple sclerosis are thus entirely analogous to those observed in experimental secondary degeneration so well described by A. Jacob.

Pronounced and widespread as the nerve destruction is, the gray matter proper (of the spinal cord, large subcortical ganglions, cortical nerve cells) is hardly involved. As a rule, the cell bodies are normal, but they may show phenomena of axonal reaction, neuronophagia, chromatolysis, pigment and fat accumulation, etc. Whatever changes the ganglion cells may exhibit, they are insignificant compared with those of the white substance and may justly be considered as secondary or accidental.

As secondary phenomena should also be considered the changes displayed by the mesodermogenic elements—the pia-arachnoid, its septal prolongations, the blood vessels and the choroid plexus.

The pia-arachnoid was always changed—thickened and infiltrated (Fig. 10). The thickening was closely associated with hyperplasia of its constituent elements (mesothelial and connective tissue cells), while the infiltration consisted of lymphocytes, plasma cells, polyblasts, gitter cells, many fibroblasts and also mesothelial cells. The majority of the infiltration elements were greatly changed, the lymphocytes, for instance, showing as dark, pyknotic nuclei, without any vestige of

10. Popoff, M.: Zur Histologie der disseminierten Sklerose des Gehirns und Rückenmarkes, Neurol Centralbl., 1894, No. 9.

11. Doinikow, B.: Ueber De-und-Regenerationserscheinungen an Achsenzylindern bei der multiplen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**: 151, 1914.

12. Dawson speaks of six and Klingman of five stages which Klingman does not consider consecutive, while Dawson says the process does not always follow the same uniform course of development.

cytoplasm, while the plasma, as well as the gitter cells, were broken up and disintegrated. In addition, there were many red cells and macrophages packed with blood pigment.

The cellular elements and their fragments were freely scattered in the meshes of the pia-arachnoid and in some instances were so densely gathered that the affected region resembled that of a meningitis.

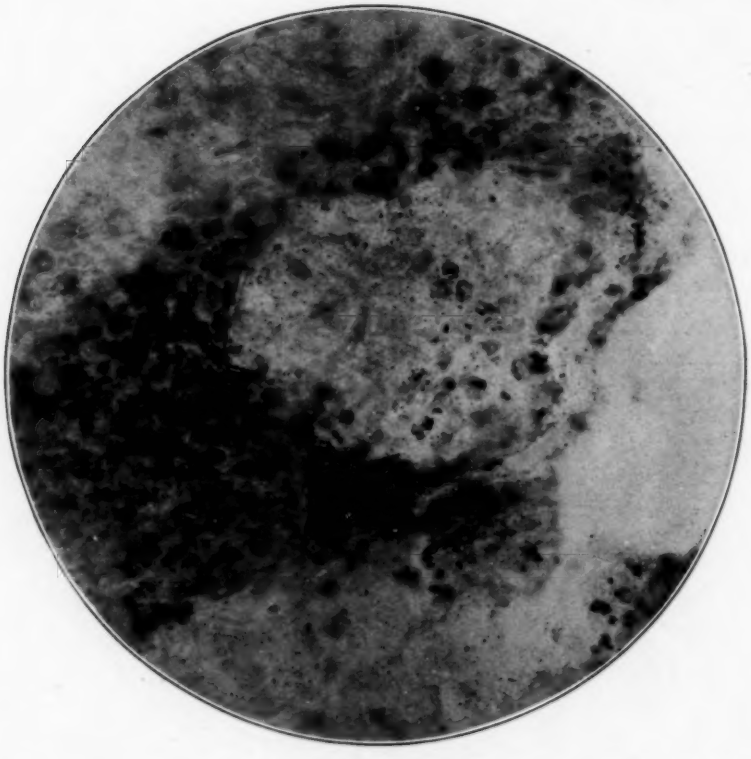

Fig. 12.—Fat accumulation in the pia (surface frozen section stained with scarlet-red-hematoxylin). Herxheimer stain; ×275.

The same hyperplasia and thickening, but without marked infiltrations, were present in the septal and cerebral prolongations of the pia, in the optic chiasm (Fig. 11) and in the blood vessels. Scarlet red and similar staining methods revealed, in both the pia and its vessels, masses of fat droplets enclosed within gitter and mesothelial cells. In some regions the pia was so densely packed with lipoid masses that these completely overshadowed other structures (Fig. 12).

As noted previously, vascular changes were present in apparently healthy regions, in the intermediate zone and in the patches themselves.

In other words, regardless of the condition of the nerve tissues and the degree and extent of the lesion, the vascular changes were alike—distended adventitial spaces packed with gitter cells, hyperplasia and thickening of their walls. Some areas, especially in the cortex, showed a greater wealth of capillaries, but no signs of budding, no regressive changes (such as hyaline degeneration, for instance), no marked thrombi formation, and only exceptionally—inflammatory cells (lymphocytes, plasma cells, polyblasts, etc.). Nor were hemorrhages with

Fig. 13.—Choroid plexus; fat globules in the tuft cells (black dots). Herxheimer stain; × 230.

reactive phenomena found, though occasionally pigment was present within macrophages found around smaller capillaries. (It was not possible to determine whether the pigment was fat or came from the blood.)

The choroid plexus (Fig. 13) invariably showed thickened vessel walls, absence of inflammatory phenomena and many fat globules within the tuft cells.

## GENERAL SUMMARY

1. There were regressive and progressive ectodermogenic changes (nerve degeneration and glia proliferation) associated with pronounced

proliferative mesodermogenic changes (hyperplasia and thickening of the vessel walls, of the pia and the septums; dilatation of the adventitial spaces and their infiltration with gitter cells).

2. Absence of significant ganglion cell changes, of inflammatory phenomena and of any relationship of the nerve changes to the territorial blood supply was noted.

3. There was an abundance of lipoids in the pia-arachnoid and in the choroid plexus.

## DISCUSSION

Of the foregoing phenomena, the most striking are the ectodermogenic changes. They show primarily as a nerve degeneration which goes through the same successive stages and obeys the same laws so well brought out by A. Jacob in experimental secondary nerve degeneration. He showed conclusively that the various morphologic glia changes, the formation of cytoplasmic glia, myeloclasts, myelophages, gitter cells and glia scar are all secondary phenomena, following a primary nerve destruction. The morphology of the glia and the type of its constituent elements (cell bodies and fibers) thus depend on the extent and severity of the parenchymatous lesions; in other words, the condition of the glia tissue denotes how far the nerve destruction has advanced.

The rôle of the glia, however, is not only to replace a destroyed parenchyma, but actively to remove it from the organism through the process of digesting the broken up nerve fragments and transforming them into harmless lipoid substances. When this is accomplished, the lipoids enclosed within gitter cells are carried to the adventitial spaces of the blood vessels and thence to the subarachnoid space.

In both the subarachnoid and the adventitial spaces, the fat laden gitter cells, as foreign bodies, cause an active proliferation of the constituent mesodermogenic or adventitial elements resulting in distention of the connective tissue meshes. With the removal of the invaders to the blood stream, the hyperplastic connective tissue of the blood vessel walls and the pia collapse and shrink, thus causing their thickening. The shrinking of the vessel walls may be so extreme as to cause a complete or partial separation of the vessels from the surrounding glia tissue and lead to formation of so-called His spaces, designated by Nissl and his school as "Schrumpfraume" (contraction spaces). Or the shrinking may be gradual and lead merely to the rarefaction of the adjacent glia with distention of its meshes, in short, to sievelike or "areolated areas." Such conditions (His spaces and areolated areas) have been considered by Borst [13] as the primary, essential cause of a patch formation. Without going into lengthy discussions of such a

13. Borst, M.: Die multiple Sklerose des Zentralnervensystems, Ergebn. d. allg. Pathol. u. pathol. Anat. **9**[1]:66, 1904. Zur pathologischen Anatomie und Pathogenese der multiplen Sklerose des Gehirns und Rückenmarks, Ziegler's Beitr. z. pathol. Anat. u. allg. Pathol. **21**:308, 1897.

view, I wish to point out that similar conditions also occur in any brain, whether normal or pathologic, and that in multiple sclerosis the spinal cord, so rich in patches, does not show them at all. The phenomena outlined as observed in the adventitial lymph spaces, in the pia and in the perivascular areas, are purely secondary or accidental. They are found in areas devoid of patches and may be absent in regions profoundly changed, for they are due to the harboring of the destroyed parenchyma while on its way from the focus of destruction to the subarachnoid space. Distended adventitial spaces packed with gitter cells occur in any pathologic condition in which secondary degeneration is the principal feature, as, for instance, in amyotrophic lateral sclerosis, subacute combined cord degeneration and secondary cord degenerations. In short, the vascular, the pial and perivascular changes are not specific for multiple sclerosis and therefore cannot be considered the cause of the patch formation, its growth or dissemination. Nor does the patch follow the course of a blood vessel as Dawson and others have shown. Dawson,[8] for instance, studied small foci of sclerosis serially throughout their whole extent and came to the conclusion that they do not coincide with the vascular areas at all.

As the principal or primary changes are parenchymatous and are confined to the nerve fibers, while those in the glia and mesodermogenic elements (vessels, pia, its septal prolongations) are secondary, it follows that were it possible experimentally to produce multiple sclerosis, connective tissue changes would be found, but as purely accidental, nonessential phenomena. So far, experimental multiple sclerosis has not been produced, nor is it possible to produce this disease either by interference with the blood supply or by irritation of the spinal cord.

Attempts to produce multiple sclerosis by injecting (intravenously, subcutaneously or intraperitoneally) spinal fluid from corresponding patients are theoretically fully justified. For such a cerebrospinal fluid discharged into the subarachnoid space is saturated with the products of catabolism or toxins which are the most probable cause of this morbid condition. The histopathologic findings are certainly quite typical of a toxic, not a microbic, lesion and do not resemble the lesions resulting from disturbed blood circulation.

Vascular disturbances, of the nature of embolism and thrombosis, may produce foci of necrosis with subsequent formation of foci of sclerosis. But such secondary sclerotic foci have little in common with those seen in multiple sclerosis. The same is true of the patches resulting from local irritation of the spinal cord substance. Thus, Leyden [14] by injecting liquor potassii arsenitis (Fowler's solution) into the spinal cord of dogs produced what he thought to be patches analogous to those seen in men, and he concluded that multiple

14. Leyden, E.: Ueber experimentell erzeugte Rückenmarkssklerose und die Ausgänge der Myelitis, Charité Ann. **3**:248, 1876.

sclerosis is the result of a myelitis. Westphal,[15] discussing Leyden's experiments, justly remarked that not every patch is to be considered the result of a previous inflammation.

In other words, patches occurring in the central nervous system may be of various origins. Weigert-Pal stain, for instance, may show patches in cerebrospinal syphilis, disseminated encephalomyelitis, general paralysis of the insane, arteriosclerosis of the brain, traumatic cord and brain lesions, in short, whenever and wherever the parenchyma is directly involved. These morbid conditions may clinically and pathologically so much resemble multiple sclerosis that they have many times been mistaken for it by both clinicians and pathologists. The patches in the foregoing diseases, however, differ greatly from those seen in multiple sclerosis. Some will show inflammatory phenomena, as in encephalomyelitis, some will exhibit areas of softening, or, in addition to glia changes, also marked connective tissue proliferation (in syphilitic lesions), etc. In short, they will exhibit phenomena entirely foreign to the conditions seen in multiple sclerosis and on the other hand there will be lacking the characteristic features.

For multiple sclerosis has a pathologic constant in its pathogenesis, the changes starting as tumefaction of the myelin which, followed by the destruction of the axon, ultimately results in secondary degeneration —they begin as a periaxial neuritis and end as wallerian degeneration. The disease constantly affects new fibers which ultimately become replaced by a glia tissue scar. It resembles only subacute combined cord degeneration and peripheral nerve lesions caused by lead, alcohol or other poisons, described by Gombault,[4] Stransky[5] and especially well by Doinikow.[6]

Multiple sclerosis also resembles a peculiar morbid condition which I am now studying in which the dominant feature is also a degenerative process, but in which the changes are limited to the second stage.

## CONCLUSIONS

1. In multiple sclerosis there are definite early changes in the form of widespread swelling of the myelin substance.

2. The myelin alteration is an acute and early manifestation with the formation of a waxy patch.

3. The glia undergoes changes later.

4. The pathologic changes are primarily ectodermogenic, the mesodermogenic tissue participating in the alterations of the disease secondarily.

5. Vascular and septal changes are present, but are accidental phenomena.

6. Theoretically it is possible to produce the changes of multiple sclerosis without concomitant changes in the connective tissue elements.

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15. Westphal: Berl. klin. Wchnschr. **15**:121, 1878.

7. The patches of sclerosis are not representative of territorial areas in relation to the arterioles, the venules and the perivascular lymph drainage.

8. The lesions of multiple sclerosis cannot be produced experimentally either by interference with, or irritation of, the vascular supply or the spinal cord.

# AN INVESTIGATION OF THE AXIS CYLINDER IN ITS RELATION TO MULTIPLE SCLEROSIS *

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It can no longer be doubted that in both the acute and chronic form of multiple sclerosis, the axis cylinder suffers distinct injury. On the other hand, no one will be inclined to doubt that in the presence of greatly advanced sclerotic patches, despite the advanced disintegration of the medullary substance, in both recent and old plaques, axis cylinders are still preserved. However, several questions regarding the axis cylinder are still unanswered, which by the application of modern methods of investigation may in time be cleared up.

What follows applies to a number of questions concerning the axis cylinder. The method used is that of Jakob (anilin blue and gold orange method, according to Mallory) which allows a distinct differentiation between the axis cylinder, the medullary sheath and the glia in the same section. We have also examined sections stained by the Bielschowsky method, for comparison—sections taken from acute cases, as well as from those in which the changes were frankly sclerotic. The changes the axis cylinder undergoes in multiple sclerosis are approximately the same as those described by Marburg [1] in the acute types of this disease. The outstanding features are thickening, globular distention, vacuolization, disintegration and, in the older sclerotic areas, the appearance of thin threads. One sees occasionally separated fibrillae pushed up or scattered along the periphery.

The absence of secondary degeneration in axis cylinders showing such serious deterioration is striking. It is possible that we are here confronted with certain edemas that are reversible in nature to a certain extent in the acute cases and to a less degree in the chronic types. Marburg has drawn a parallel between the changes observed in the medullary sheath in multiple sclerosis and those found in peri-axial neuritis of the Gombault-Stransky type. According to him, the medullary sheath breaks up first, the axis cylinders remaining com-

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* This work was done in the Neurological Institute, Vienna, under Prof. Otto Marburg.

* Read before the Association for Research in Nervous and Mental Diseases at its Second Annual Meeting, Hotel Commodore, New York, Dec. 28-29, 1921.

1. Marburg: Die sogenannte multiple Sklerose, Liepzig and Vienna: Deuticke, 1906; Multiple Sklerose, Handbuch der Neurologie, Berlin: Springer, **12**: No. 1, 1911.

paratively uninjured. This type of medullary disintegration, heretofore unknown in the central nervous system, has since been demonstrated by Shimazono [2] in animals subjected to experimental lead poisoning. In Shimazono's sections, however, one is impressed with the fact that the axis cylinder is not distended and edematous as observed in multiple sclerosis, but rather broken up into rows of granules, having previously become narrower and thinned out.

Kimura,[3] in his investigation into the degenerative and regenerative processes of the peripheral nervous system, reports similar changes, and he greatly restricts the term periaxial degeneration. This investigator also believes that primarily the axis cylinder is mostly injured in the neuritides. It is true he does not preclude the destruction of the medullary sheath around the still existing axis cylinder, yet he assumes that to bring this about there must be a serious lesion of the peripheral nerve. He adds, further, that in nerves in which the medullary substance has already broken up into clods, no well preserved axis cylinder is to be found. Since the axis cylinder perishes before the medullary sheath is entirely broken up, we must assume that a long smooth axis cylinder when seen in the field is formed of vacuolated fibers, at least as far as the peripheral nerves are concerned. This apparently contradicts the existence of a periaxial neuritis type of reaction.

Siemerling and Raecke,[4] in their comprehensive studies, maintain that the lesion of the nerve is primarily manifested in the axis cylinder. They believe the process originates in the vascular system, an hypothesis adopted by Fraenkel and Jakob,[5] who base their opinion on a study of the smallest areas just developing. A process originating in the vascular system and chiefly affecting the medullary sheath has been known for some time. This manifests itself particularly in pernicious anemia, in which the pathology of the changes has been by no means ascertained. It is attended by complete destruction of all the nerve fibers within a limited area.

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2. Shimazono: Ueber das verhalten der zentralen und der peripherer Nervensubstanz bei verschiedenen Vergiftungen und Ernährungsstörungen, Arch. f. Psychiat. **53**:972, 1914.

3. Kimura: Histologische degenerations und regenerations Vorgänge im peripheren Nervensystem, Mitteilungen aus dem path. Inst. der Kais., Japan. Universität zu Sendai **1**: No. 1, 1919.

4. Siemerling and Raecke: Beitrag zur Klinik und Pathologie der multiple Sklerose mit besonderer Berücksichtigung ihrer Pathogenese, Arch. f. Psychiat. **53**:385, 1914.

5. Fraenkel and Jakob: Zur Pathologie der multiplen Sklerose mit besonderer Berücksichtigung der akuten Formen, Ztschr. d. ges. Neurol. u. Psychiat. **14**: 565, 1911.

Shimazono, and more recently Wohlwill[6] have shown that in pernicious anemia the axis cylinder primarily is injured. The medullary sheath is at first only passively stretched. The glia then begins to proliferate by way of reaction and seemingly compresses the axis cylinder which it eventually absorbs after its disintegration; while the medullary sheath disintegrates in its turn, not into large clumps, but into small particles. At the same time a narrow line of medullary sheath attaches itself to the heavily degenerated axis cylinder.

We have, therefore, two distinct processes affecting the nerves—the one alleged to begin in the axis cylinder, the other in the medullary sheath. The existence of the latter cannot possibly be doubted if we examine longitudinal sections in multiple sclerosis. One may actually see the axis cylinder becoming uncovered and then recovered again at the far end of the small area. The line of thought pursued by

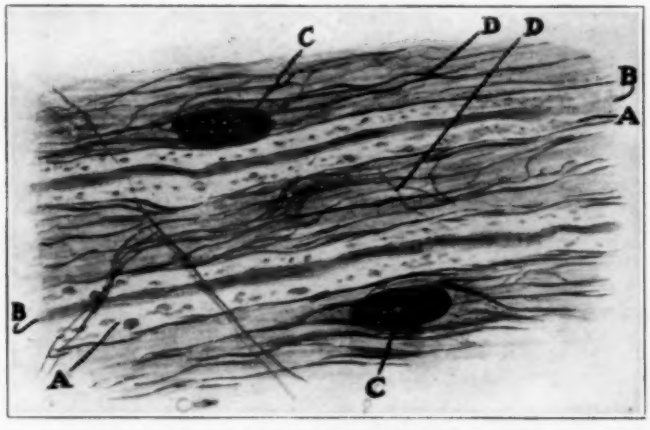


Fig. 1.—A well advanced stage of myelin disintegration; glia cells with pigment. *A*, myelin fragments; *B*, axis cylinders fairly uniform, although myelin disintegration is advanced; *C*, glia cells with pigment, broken down lipoids; *D*, glia fibers. Mallory stain, Jakob modification; oil immersion; ocular 8.

Kimura is hardly justifiable. He assumes that a serious lesion exists remotely in the correlative nerve.

Apparently there is only one difference distinguishing experimental neuritis from the periaxial type accompanying multiple sclerosis—comparative slenderness of the axon and granular disintegration occurring overwhelmingly in the former while in the latter there is mostly swelling and distention.

6. Wohlwill: Zum Kapitel der pathologisch-anatomischen Veränderungen des Gehirns und Rückenmarks bei pernicioser Anemie und verwandten Affektionen. Deutsch. Ztschr. f. Nervenh. **68-69**:438, 1921.

Anton and Wohlwill: Multiple nichteitrige Encephalomyelitis und multiple Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **12**:31, 1912.

The question is whether the axis cylinder is primarily injured and the medullary sheath secondarily or vice versa. This cannot be decided from the study of histologic pictures alone. Examination of Jakob's slides shows that in the advanced stages of the majority of the cases the medullary sheath is completely destroyed, except that occasionally remnants are distinctly visible, a yellow tinted margin lying along the periphery of the axis cylinder. Occasionally even a nerve is found, as described by Wohlwill in cases of pernicious anemia, with an inflated axis cylinder and a relatively thin but as yet intact medullary sheath.

In both acute and chronic cases we see what Doinikow [7] has exquisitely shown—the button or globe-shaped inflations, either forming a

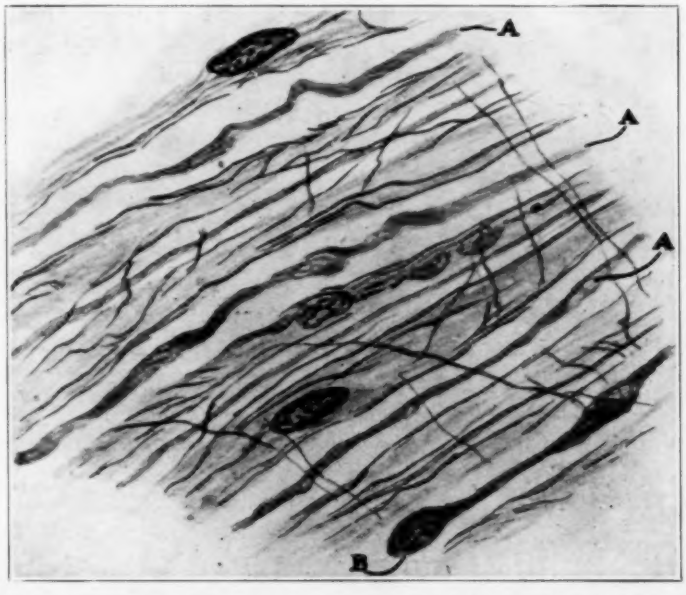


Fig. 2.—The myelin has entirely disappeared. The axis cylinders are surrounded by glia fibers. *A*, naked axis cylinders, uniform caliber gone, distorted in shape and showing vacuolization; *B*, an inflated end bulb type. Mallory stain, Jakob modification; oil immersion; ocular 8.

club shaped nerve end or a globular distention along the axons. This is also mentioned by Minea.[8] A second question is that of regeneration of the axis cylinder. The following has been demonstrated in the Vienna

7. Doinikow: Ueber De- und Re-generationserscheinungen an Achsenzylindern bei der multiple Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:151, 1915.

8. Marinesco and Minea: Nouvelles contributions a l'étude de la régénescence des fibres du système, nerveux central, J. f. Psychiat. u. Neurol. **21**:116, 1910-1911.

Neurological Institute, by Miyake.[9] Only one day after complete section of the spinal cord, these spherical bodies and inflations were observed on the axis cylinders; that is, at a period when regeneration can hardly be considered. Consequently, it is impossible to infer that these tumefactions are indicative of regeneration. However, threadlike processes or fibrillae sprouting out of the globular distentions may perhaps be an indication of beginning regeneration, but regeneration would by no means account for the preservation in many areas of considerable numbers of naked axis cylinders still capable of conduction. Disintegration of the medullary sheath with comparative intactness of the axis cylinder must be regarded as a specific characteristic of multiple sclerosis. An explanation of the peculiar relationship between the axis cylinder and the medullary sheath may be found in the work of Spiegel of Vienna, who showed that every lesion of the medullary sheath must be followed by one in the axis cylinder for physico-chemical reasons.

The polarization microscope has shown us that the edematous nerve may return to its normal condition, providing the noxious influence has ceased to exist. The inference is that if the noxious influence continues, a lesion of the axis cylinder supervenes, and the degree of impairment of function depends on the degree of this lesion. This work tends to show that in pernicious anemia toxins injure primarily the axis cylinder. The form of disintegration of the medullary sheath in these two diseases is different. In pernicious anemia it is in small granules; in multiple sclerosis in coarse lumps. Presumably the different types of lesions are due to different poisons, not to varying strength of the same toxin.

In multpile sclerosis the neuroglia is comparatively free from serious involvement. An excessive fibrillar growth is its most striking feature, the axis cylinder becoming surrounded by a sheath of glia, a sort of envelop of delicate network.

## CONCLUSIONS

1. The axis cylinder is damaged and may be destroyed.
2. Frequently the axis cylinders survive the lesion and the primary edema is followed by a subsidance of the same.
3. The medullary sheath is more seriously involved than the axis cylinder. It may be completely destroyed while comparatively well preserved axis cylinders remain.
4. The medullary sheath may be preserved, at least in part.
5. We accept Spiegel's conception that disintegration of the medullary sheath is accompanied by edema of the axis cylinder.

Harvey Building, 355 East 149th Street.

9. Miyake: Zur Frage der Regeneration der Nervenfasern im zentralen Nervensystem, Arbeiten aus dem Neurologischen Institut, Vienna **14**:1, 1908.

# MULTIPLE DEGENERATIVE SOFTENING VERSUS MULTIPLE SCLEROSIS *

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Recent histopathologic studies of the central nervous system have brought to light a group of cases presenting peculiar lesions in the form of scattered foci of degeneration. These foci or plaques differ microscopically from the patches of multiple sclerosis, encephalomyelitis and similar conditions and may be the cause of many indefinite clinical syndromes. These probably include many cases described as degenerative encephalitis, disseminated encephalomyelitis, malignant or acute multiple sclerosis, poliencephalitis superior of Wernicke, and other conditions. Generally speaking, they do not conform, either clinically or pathologically, to any established morbid entity.

The histopathologic examination of such a case seems to justify the conclusion that we are here dealing with a disease group *sui generis* which we propose to designate as multiple degenerative softening in order to emphasize the contrast with multiple sclerosis.

## CLINICAL REPORT OF A CASE (DR. BASSOE)

*History.*—A man, aged 28 years, was first in the Presbyterian hospital from June 8 to July 2, 1921, on account of an infection of the right middle finger for which he had been treated for three days previously. He was also found to have acute tonsillitis, catarrhal conjunctivitis and carious teeth. He complained of headache and generalized pain. At this time the reflexes were normal. The pupils and eyegrounds were normal. Vision was not taken as there was no complaint relating to it. During this stay in the hospital his weight decreased from 127 to 112 pounds.

He was readmitted ten days later, on July 12, complaining of frontal headache, failing vision, general weakness, difficulty in starting urination, spells of dizziness and ringing in the ears. Vision began to fail one week before admission. There had been no diplopia. On July 12 the blood pressure was: systolic, 92; diastolic, 64. There were 5,100,000 red cells, 8,200 white cells, and 94 per cent. hemoglobin. He could count fingers at 3 feet (91.4 cm.) with the

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* Presented before the Chicago Neurological Society, Jan. 19, 1922.

* From the pathologic laboratories of the Cook County Hospital and Illinois State Psychopathic Institute.

right eye and read ordinary print at arm's length with the left eye. The right pupil was dilated, the left of normal width; both reacted sluggishly to light and fairly in accommodation. The neck was rather stiff. The knee, elbow and wrist reflexes were relatively increased on the left side. Touch sense was normal, pain sense slightly impaired in the left leg.

Lumbar puncture yielded a clear fluid with negative Wasserman, Ross-Jones and Lange gold tests and a cell count of 5. The Wassermann test with the blood was also negative. Heart and lungs were normal.

*Examination.*—July 16: The pupils were rather wide and equal. The sense of smell was preserved on both sides. A watch was heard at 5 inches (12.7 cm.) on the right, not on contact on the left. There was no definite facial palsy. The patient could not raise his head from the pillow; attempted passive flexion of the neck caused pain, but there was no resistance to rotation. Shrugging of the shoulders and arm movements were very strong, but he could not raise himself to a sitting posture without the aid of his arms. The bladder was greatly distended. Abdominal reflexes were not obtained. Elbow and knee reflexes were brisk; ankle reflexes were normal. The patient had difficulty in placing the heel on the opposite knee, more on account of weakness than ataxia. He had to be catheterized in the evening but voided the next day.

*Course of Disease.*—July 18: Roentgenologic examination of the head: "Definite evidence of digital impressions in the anterior portions of the skull, also suggested in the parietal and temporal regions. The anterior and posterior clinoid processes appeared to be fused. Sella very small."

July 18: Leukocytes, 20,800. The temperature since admission had varied between 97.2 and 99.4 F.; the pulse between 72 and 92; respiration, 18.

July 19: Vision: With the right eye he counted fingers at 6 feet (1.82 meters); with the left eye, at 15 feet (4.56 meters). The fields were slightly contracted. Pupillary reaction to light was sluggish, more so on the right. The media was clear and the fundi normal. No muscular paralysis was present. Spontaneous nystagmus developed on deviation of the eyes in any direction. Hearing was present in both ears. Vestibular tests could not be made on account of the patient's weak condition.

July 24: Urination was frequent and burning, and there were many leukocytes in the urine. The neck was stiff as before. The left pupil was slightly larger than the right. The grip of the left hand was weaker than that of the right hand.

July 25: The patient was more somnolent. The reflexes varied from hour to hour, particularly the knee jerks. The left pupil and palpebral fissure were larger than the right. He was somewhat irrational. Slight internal strabismus and facial palsy on the left were present.

July 27: The patient had an attack of Cheyne-Stokes breathing during which the pulse became imperceptible.

The temperature did not exceed 100 F. until July 28, when it rose quickly from 99 to 104.8 F. before death on July 30.

*Diagnosis.*—No definite clinical diagnosis was made. Among the conditions most seriously considered were tumor or inflammation of the hypophysis, frontal lobe abscesses and some form of encephalitis.

*Clinical and Gross Necropsy Findings.*—These findings were: an acute infection followed by headache, vertigo, failing vision and urinary distress with retention. The somewhat indefinite neurologic findings were: unequal, sluggish pupils, slight rigidity of the neck, inconstant reflexes which varied from hour

to hour, slight facial paralysis, strabismus and nystagmus. The course was acute and afebrile (except for terminal hyperpyrexia) and resulted in death seven weeks after the onset.

At necropsy the anatomic diagnosis by Dr. B. O. Raulston was: extensive right bronchopneumonia; acute right fibrinous pleuritis; encephalitis; edema of the meninges and brain; anemia and emaciation; moderate atheromatous changes of the aorta; fatty changes of the liver; narrowed cortices of the suprarenal glands; moderate hypertrophy of the spleen; fibrous adhesions between the spleen and the omentum, the vermiform appendix and the mesentery of the cecum; petechial hemorrhages in the gastric and duodenal mucosa, the renal pelvis and urinary bladder; acute hyperplasia and partial calcification of the tracheobronchial lymph glands; small accessory spleen.

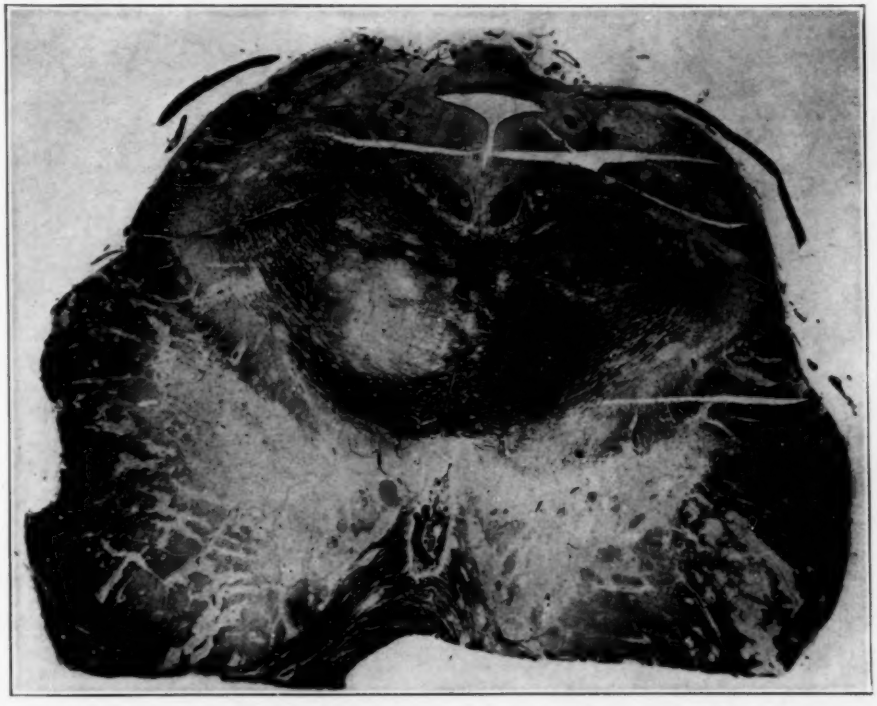

Fig. 1.—Soft patch in the decussation of the brachia conjunctiva. Weigert-Pal stain; × 4.

### Histopathologic Examination (Dr. Hassin)

The brain, received in 10 per cent. formaldehyd, had been cut into small pieces. Macroscopically these appeared entirely normal, there being no evidence of hemorrhage, abscess, focal softening, meningeal or ventricular change.

After embedding in celloidin and staining with various methods, distinct patches were discovered in the medulla oblongata, pons, corpora quadrigemina, nucleus dentatus cerebelli and nucleus caudatus. Figure 1 shows such a patch in the pons where it occupied the left half of the decussation of the brachia conjunctiva. It appeared pale, round and sharply defined, greatly resembling a patch of multiple sclerosis.

Histologic examination, however, revealed marked differences. Figure 2 shows such a patch stained with toluidin blue. It consisted of a mass of cellular elements of exclusively gliogenous origin (myelophages and various types of gitter cells). Under a higher power (Fig. 3) they appeared markedly vacuolated and, in specimens stained with scarlet red, were seen to be filled with fat. The areas at the margin of the patches contained large cytoplasmic glia cells with numerous ramifying processes and an eccentric nucleus, rich in chromatin. There were many blood vessels, mostly small capillaries, distended with blood and possessing somewhat thickened walls with prominent and well stained endothelium and dilated adventitial spaces packed with gitter cells. Nerve fibers,

Fig. 2.—Soft patch in the region of the nucleus dentatus cerebelli, consisting of a mass of cell bodies represented under a higher power lens in Figure 3. Within the patch and surrounding the same are numerous small vessels and capillaries infiltrated with gitter cells. Toluidin blue; × 40.

fragments of myelin, Marchi globules and ganglion cells could not be found in the foci. Briefly, certain portions of the brain had been transformed into glia cells laden with lipoid substances, a phenomenon typical of secondary nerve degeneration.

Other areas were noteworthy, not so much for foci of degeneration as for the presence of a great wealth of blood vessels. Thus, the cerebral peduncles, the substantia nigra, the areas around the third and fourth ventricles and the medulla, all showed markedly infiltrated blood vessels (Fig. 4). At first glance they strikingly resembled the vascular condition seen in epidemic encephalitis; but

when stained by the methods of Alzheimer-Mann, Bielschowsky and Herxheimer, the infiltrating elements proved to be principally gitter cells (Fig. 5). While in smaller vessels (Fig. 6) and capillaries these were the only types of cell found, in the adventitial spaces of larger vessels the gitter cells were intermingled with cells resembling lymphocytes. They were, however, homogeneous in appearance, pyknotic, without chromatin or cytoplasm. Cells indefinitely resembling plasma cells were also present but less common. In other words, while neither plasma cells nor lymphocytes could be recognized with certainty, their presence could not be excluded.

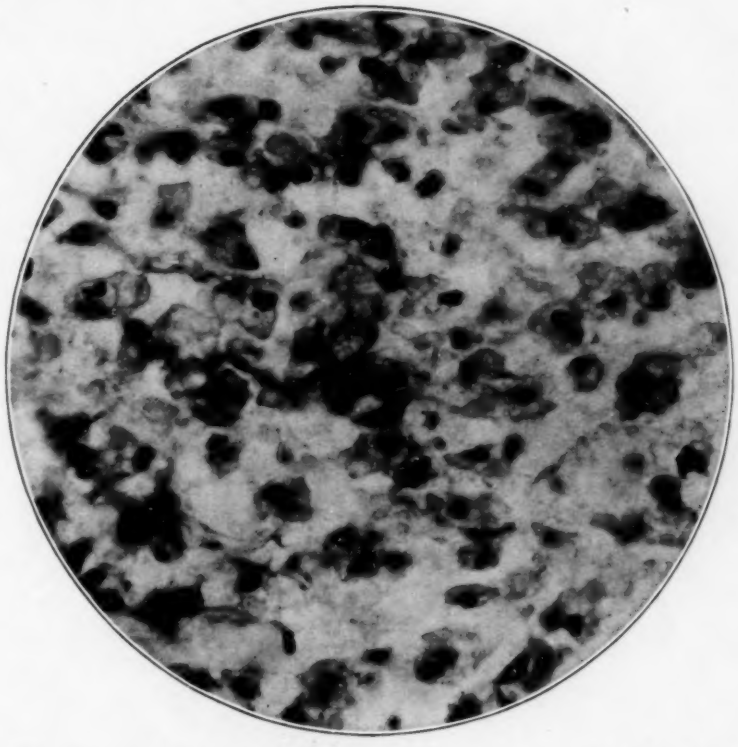

Fig. 3.—Same as Figure 2. Myelophages (large vacuolated bodies) and gitter cells. Use hand lens. Toluidin blue; × 490.

Some blood vessels and capillaries appeared quite normal, that is to say, without perivascular infiltrations, while in other rare instances there were indications of young and new-formed capillaries.

The ganglion cells, in the neighborhood of the foci, were more or less changed. The majority contained pale, chromatin-poor nuclei (as if undergoing dissolution or karolysis) and were provided with thick, tortuous, densely stained processes. Some cell bodies were somewhat swollen, or broken up and invaded by glia cells (neuronophagia). Others were distinctly vacuolated or sclerosed and shrunken with flattened nucleus, while the majority were packed with fat. In other words, karyolysis, neuronophagia and fatty cell degeneration were the prominent phenomena in the areas of the brain containing the foci of degenerative softening.

Equally pronounced were the changes in the basal ganglions (optic thalamus and nucleus lenticularis), the subcortical white substance, the cerebral cortex, cerebellum and especially the optic chiasm. These regions contained no patches but exhibited instead, especially in the neighborhood of blood vessels, numerous foci or clusters of glia nuclei (Fig. 7). The majority were of large size, rich in chromatin, and for the most part had a generous amount of cytoplasm. On the other hand, some glia nuclei, though somewhat large in size, were rather poor in chromatin and appeared pale and quite devoid of cytoplasm. The cytoplasmic glia cells frequently merged to form rosettes (Fig 8). These were quite frequent around or within the fat laden ganglion cells (Fig. 8).

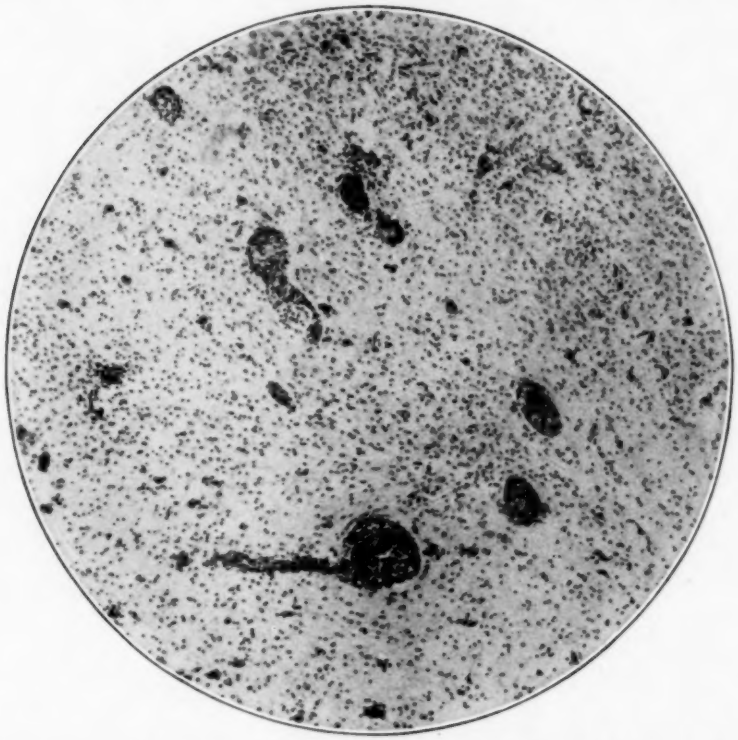

Fig. 4.—The region of the cerebral peduncles. Marked infiltration of blood vessels and capillaries resembling that seen in lethargic encephalitis. Some of the infiltration cells are reproduced in Figures 5 and 6. Use lens. Toluidin blue; ×70.

An interesting feature was the presence of rod cells (Stäbchenzellen) in the form of curved, sausage-like cell bodies supplied at their poles with slender processes. They were found not only in the cortex, but also in the subcortical areas and in the basal ganglions (Fig. 8). These regions were richly supplied with blood vessels, mostly capillaries, having lipoids in their perivascular spaces, but without other pathologic changes (thrombi, endarteritis, hyaline degeneration).

The nerve cells of the cortex and the basal ganglions showed changes which were somewhat similar to those already outlined. Especially noteworthy were accumulations of fat in the cell bodies (Fig. 9) and satellitosis in the form of rosette formation. Such cell changes involved every lobe of the brain, as well as every layer, though the deeper cortical strata were particularly affected.

Fatlike substances were also present in the glia cells and the capillary walls, and sections stained with scarlet red presented appearances characteristic of parenchymatous degeneration, well shown in Figure 10.

Lipoids were equally common in the pia-arachnoid all over the cortex and were mixed with a great number of lymphocytes, polyblasts, fibroblasts, and

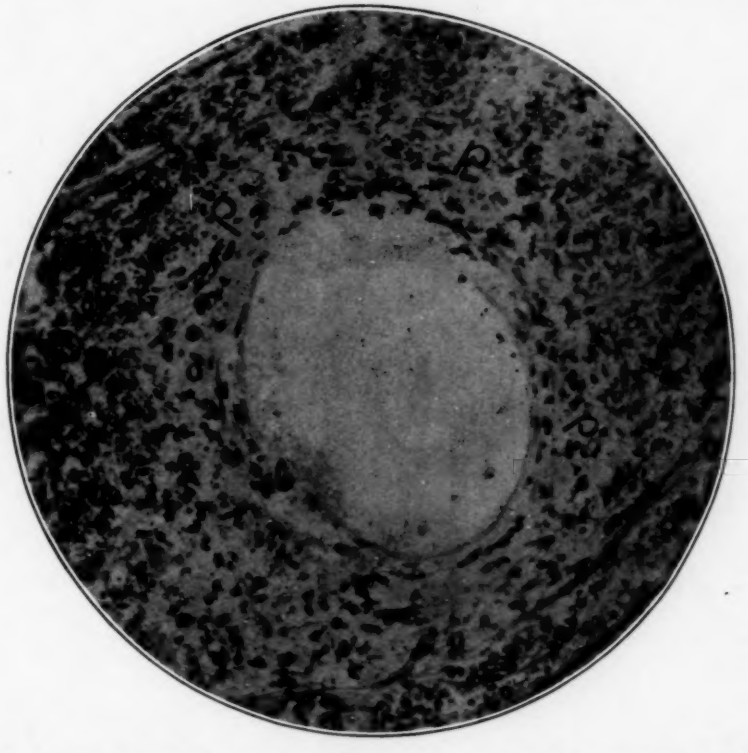

Fig. 5.—Nucleus caudatus: large vein infiltrated with fat granule cells—black stained cell bodies in the perivascular space, *p*, *p*, *p*. Herxheimer scarlet red; × 150.

mesothelial cells. All these elements were scattered within the distended meshes of the subarachnoid space and the capsule of the pituitary body. The choroid plexus likewise showed drops or droplets of fatlike substances, especially within the tuft cells.

Only the upper portion of the cervical region of the spinal cord was available for study. It showed no signs of secondary degeneration. The changes were similar to those found in the cortex: absence of large degenerative foci, presence of foci of glia nuclei, ganglion cell degeneration and absence of definite inflammatory phenomena.

The microscopic examination of the viscera and the pituitary body revealed no findings of special interest.

SUMMARY OF THE PATHOLOGIC FINDINGS AND DISCUSSION

The pathologic findings were:

1. Foci of degeneration in the midbrain, medulla and to a less extent in the nucleus caudatus.

2. Diffuse degeneration of the cortex, basal ganglions and the available portion of the spinal cord (cervical region).

3. Definite widespread gitter cell infiltration of the blood vessels, especially the capillaries, of the midbrain, basal ganglions and medulla.

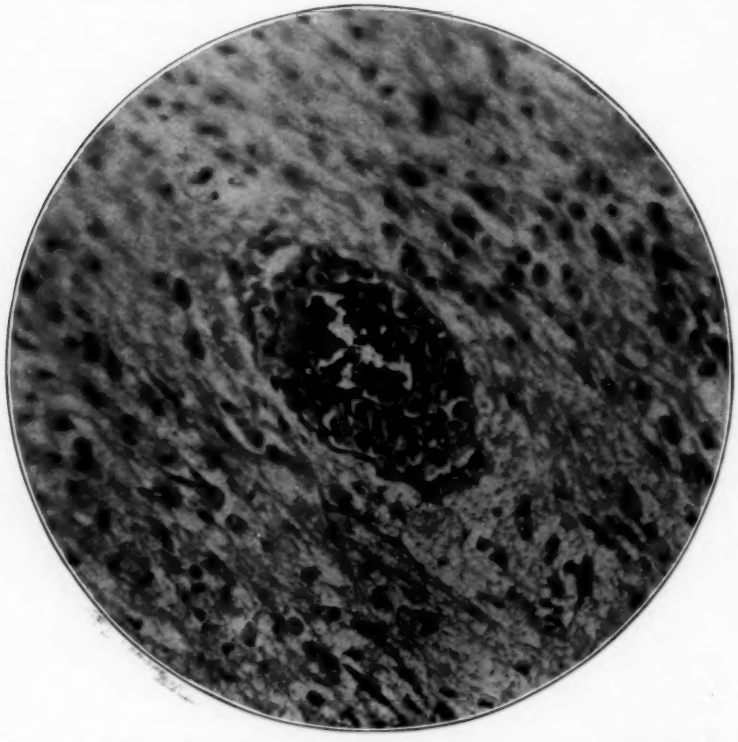

Fig. 6.—Optic chiasm: small blood vessel with numerous gitter cells in the distended meshes of the adventitial space. Bielschowsky stain; × 275.

4. Absence of inflammatory phenomena as well as of secondary degeneration in the spinal cord.

5. Reactive phenomena and presence of lipoids in the subarachnoid space and the choroid plexus.

Of the features described, the most outstanding were the patches of degeneration. As noted, grossly they resembled those of multiple sclerosis, but microscopically they differed greatly. Thus, nerve fibers, glia fibers and Marchi globules were entirely lacking, and the changes peculiar to the various stages of the evolution of a patch of multiple sclerosis were absent. The resemblance to the so-called second stage

of such a patch, pointed out in a previous article,[1] is certainly superficial. For even in this stage of multiple sclerosis there are present, not only gitter cells and similar structures, but also nerve fibers, either well preserved, or in an early stage of degeneration. The foci in the case here described were entirely devoid of nerve structures and in this respect resembled foci of ischemic softening. They differed from these, however, in that the general architecture of the component elements was preserved as it is not in ischemic foci of softening such as those caused by thrombosis. In the latter the parenchyma is entirely broken up.

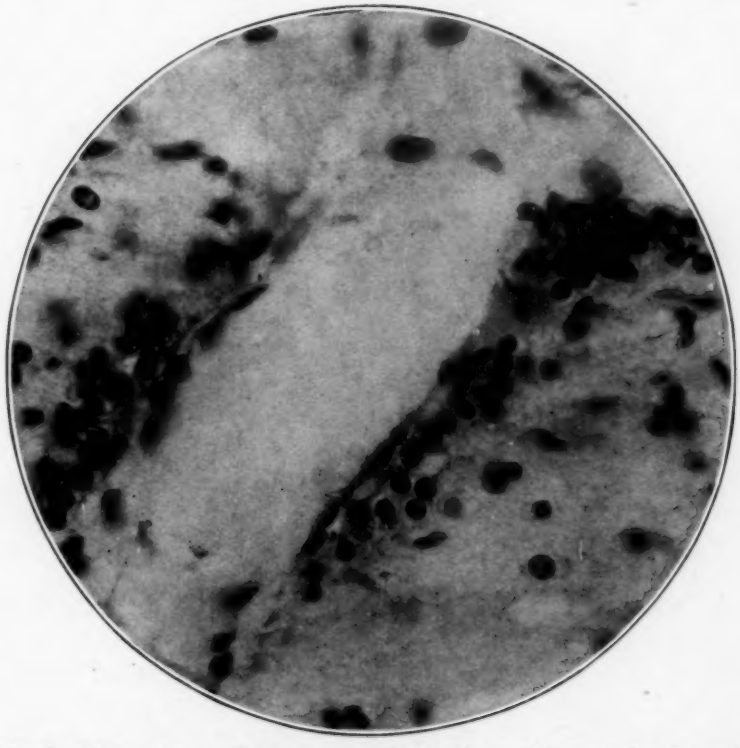

Fig. 7.—Motor area: Clusters or foci of glia nuclei around a large blood vessel. Toluidin blue; × 560.

Under the microscope the field is strewn with fragmented nerve fibers, with immense numbers of myelophages and gitter cells, many of which are crowded densely around or within the adventitial spaces of floating blood vessels. In short, the parenchyma is liquefied. The patches in this case did not show liquefaction. They were comparatively solid though much less firm than patches containing neuroglia or connective tissue. Compared with the latter, they were essentially soft, and it is in this sense that the term "softening" has been used.

1. Hassin, G. B.: Studies in the Pathogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:589 (May) 1922.

In some respects they resemble the patches described by Williamson [1a] in a case of "early disseminated sclerosis."

The patient, a young man, 23 years old, complained of paresthesias in the hands and toes followed by a successive paralysis of the upper and lower extremities. The tendon reflexes were exaggerated, with bilateral foot clonus, while the skin reflexes were absent. There was intention tremor in the hands, scanning speech and nystagmus on looking to the right; the mentality was dull. Death occurred a year after

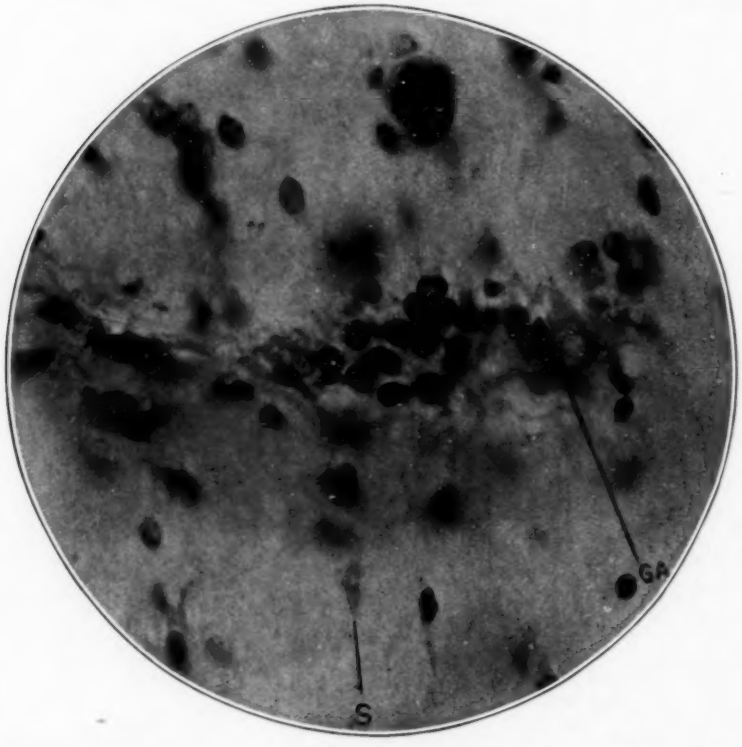


Fig. 8.—Optic thalamus: In the center accumulation of glia cells forming a rosette; *Ga*, ganglion cell invaded by glia cells (neuronophagia); *S*, Stäbchenzelle (rod cells). Use hand lens. Toluidin blue; × 560.

the onset of the first symptoms. Necropsy revealed "soft roundish grayish-yellow gelatinous semitransparent patches" in the frontal lobe, in the center of the white substance of the left occipital and right temporosphenoidal lobes. In addition, there were found a number of "firm" patches in the white matter of the cerebral hemispheres, spinal cord, crus, pons and medulla. These consisted of dense neuroglia fibers, but showed no nerve fibers. The soft patches likewise were

1a. Williamson, R. T.: The Early Pathologic Changes in Disseminated Sclerosis, The Medical Chronicle **19**:373 (March) 1894.

devoid of nerve fibers and consisted of numerous "fat-granular bodies," white and red blood cells, "scattered neuroglia" fibers and glia cells and numerous dilated vessels infiltrated with "round" cells. From Williamson's description of the "soft" patches one may gather that they were not typical of anything seen in multiple sclerosis and that in some features they resembled the patches of our case.

The latter much more closely resembles the cases of Oppenheim and Henneberg,[2] Kramer and Henneberg,[3] Redlich,[4] Schultze,[5] a case described by one of us [6] and partly the case of Alzheimer.[7]

Oppenheim and Henneberg's patient was a man, 39 years old, with a history of trauma (contusion of the back). The clinical symptoms were: Korsakoff's syndrome, slight optic neuritis, hypotonia, loss of tendon and abdominal reflexes, bilateral Babinski sign (in spite of the paralysis being flaccid), bulbar symptoms (dysarthria, dysphagia, chewing troubles), facial nerve paralysis and urinary disturbances. The remarkable feature was the variation of the reflexes, as in our case, and the hypotonia. Oppenheim concluded that the case was either acute multiple sclerosis or disseminated encephalomyelitis.

The histopathologic examination by Henneberg showed foci of softening in the corpus callosum, the adjacent hemispheres and cingulum. In the "distal portion of the pons and medulla" there was a large focus which microscopically looked like an "infiltrative encephalitis." The cerebral foci showed no axons, but many fat granule bodies enclosed within meshes of "connective tissue," large glia nuclei and small cell infiltration of some larger blood vessels. The spinal cord exhibited diffuse degenerative and inflammatory changes. Henneberg ascribes the foci in the brain to an "inflammatory softening" probably due to stasis, while those of the pons and medulla though resembling, he says, "malignant" multiple sclerosis, are rather "indicative of acute degenerative encephalitis."

Though Henneberg's conceptions of so-called degenerative encephalitis (and degenerative or funicular myelitis) are open to criticism, his views as to the nature of the so-called degenerative (funicular) myelitis

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2. Henneberg: Ueber disseminierte Encephalitis, Neurol. Centralbl. **36**:652, 1916. Oppenheim: Deutsch. Ztschr. f. Nervenh. **52**:172, 1914 (Case 1).

3. Kramer and Henneberg: Ueber disseminierte Encephalitis, Neurol. Centralbl. **36**:984, 1916.

4. Redlich, E.: Ueber Encephalitis Pontis et Cerebelli, Ztschr. f. d. gesam. Neurol. u. Psychiat. (Originalien) **37**:1, 1917.

5. Schultze, F.: Ueber Multiple Sclerose und herdförmige Encephalitis, Deutsch. Ztschr. f. Nervenh. **65**:1, 1920.

6. Hassin, G. B.: Histopathologic Findings in a Case of Superior and Inferior Poliencephalitis with Remarks on the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **5**:552 (May) 1921.

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being by no means universally accepted, he certainly was justified in rejecting Oppenheim's diagnosis of multiple sclerosis. The cellular infiltrations which he mentions, but does not describe, might have been fat-granule bodies (gitter cells), and the process thus wholly degenerative.

Kramer-Henneberg's case concerned a woman, 43 years old, who gradually developed left hemiplegia and hemianesthesia, preceded by asthenia, paresthesias, first in the left hand and then in the entire left side of the body, and diminution of taste in the left half of the tongue. All these symptoms, except slight weakness in the left hand, cleared up.

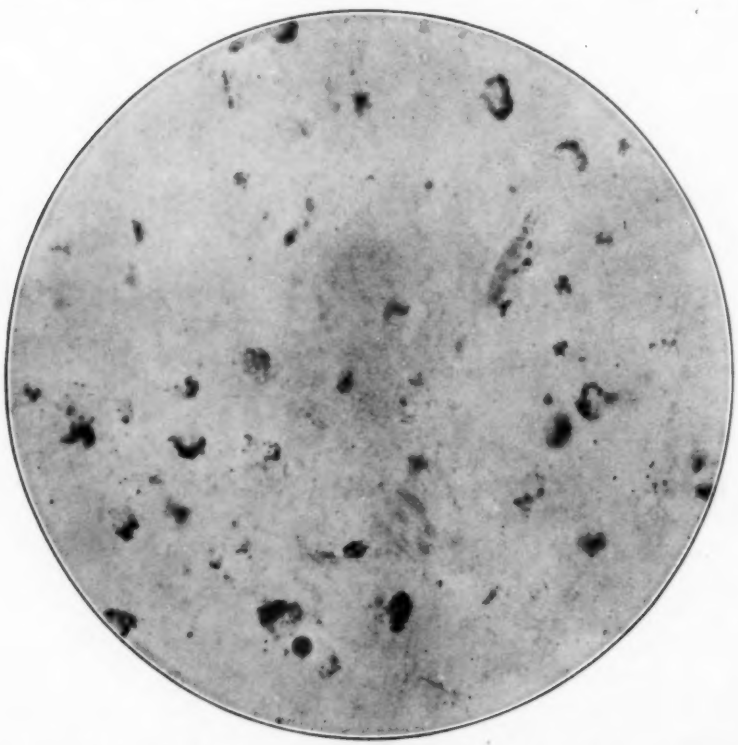

Fig. 9.—Putamen: lipoids in the ganglion cells can be distinctly seen, especially with the help of a hand lens. Scarlet red; × 275.

Three years later, the left hemiplegia and hemianesthesia returned, together with paralysis of the right sixth and seventh cranial nerves and diminution of hearing and taste on the right side. These symptoms were followed by disturbances of deglutition and speech, strabismus and diplopia. The duration of the second attack was about three months.

Necropsy revealed a focus of softening in the right hemisphere. It involved the posterior central convolution, gyrus cinguli and corpus

callosum, extending to the white substance. Another focus existed in the medulla oblongata occupying an area comprising a portion of the decussation of the pyramids, the middle of the pons, the sixth nucleus, brachia conjunctiva, mesial lemniscus and the reticular substance. Microscopically, there was no myelin, a few glia fibers and numerous gitter cells (in the medullary focus) mixed with rod cells; the vessels were infiltrated with lymphocytes which freely invaded the neighboring tissues. Henneberg is inclined to consider this case somewhat akin to malignant multiple sclerosis, but prefers to classify it as disseminated encephalomyelitis.

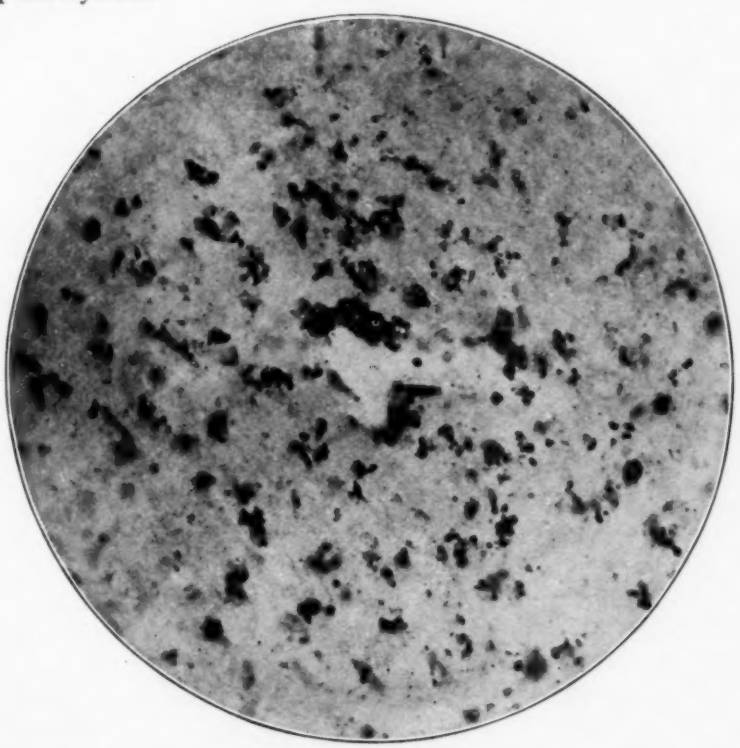

Fig. 10.—Cortex: lipoid substances in the ganglion cells, glia nuclei and around capillaries. Herxheimer scarlet red; × 230.

Redlich's patient, a young man, 20 years old, suddenly developed cerebellar ataxia, left ocular paralysis and nystagmus. Slight improvement was followed by paralysis of all the branches of the left, and then of the right, seventh nerve, ataxia in the right leg, increased tendon reflexes with bilateral Babinski sign and slight intention tremor. The duration of the illness was about five months. At necropsy there were found large foci of softening in both cerebellar hemispheres, extending through the posterior corpora quadrigemina into the pons, red nucleus

and the decussation of the pyramids. The foci of the midbrain consisted of numerous fat-granule cells, proliferated glia cells and hyperemic blood vessels infiltrated "so far as could be made out" with lymphocytes, and, possibly, with plasma-cells. Notwithstanding the predominance of degenerative phenomena, Redlich considers this case an inflammatory process; he therefore excludes multiple sclerosis and designates it "subacute interstitial or hyperplastic encephalitis of Hayem."

Schultze's patient, 43 years old, had "aphasic-dysarthric" troubles, right hemiparesis with exaggerated reflexes but without Babinski sign, disturbed sense of position in the right fingers and an uncertain gait. The condition gradually became worse and within three weeks there was complete right-sided paralysis with exaggerated reflexes and positive Babinski sign on both sides, marked disturbances of speech, deglutition and urination and mental depression. The patient had previously had two transient attacks of paralysis of the left arm, one about a year, the other about fourteen years, prior to the onset of the last illness which lasted altogether about ten weeks. Necropsy revealed numerous miliary foci in the left hemisphere (cortical and subcortical), pons and medulla, while the spinal cord appeared normal throughout. The foci contained no myelin, hardly any axons, many gitter cells and no infiltrated vessels. Neither clinically nor pathologically was the case clear to Schultze. He considered multiple sclerosis, encephalitis, "focal tissue destruction" and, as he put it, "probably an entirely new not yet described clinical entity." At any rate, he adds, it was not an inflammatory process.

In a case reported by one of us,[6] the clinical picture was a combination of poliencephalitis superior (ophthalmoplegia) with bulbar paralysis (poliencephalitis inferior). Histologically, there were extensive foci of degeneration in the medulla, pons and midbrain, combined with diffuse degeneration of the cortex and basal ganglions.

Quite unique was Alzheimer's case. A woman, 27 years old, showed mental disorder (depression and impulsive crying) with disturbances of speech, deglutition and gait. A remarkable feature was the occurrence of attacks of painful tonic muscular contractions in the left arm which would set in on attempts to talk. The muscles of the entire left arm, except those of the fingers would become hard as wood and very painful. The painful spasmodic contractions then involved the right arm and the left leg, and to prevent such attacks the patient had to avoid talking. Death occurred about three years after the onset.

Necropsy revealed combined cord degeneration, symmetrical foci of degeneration in the seventh cranial nerve nuclei and nucleus ambigus, in the globus pallidus (bilaterally), foci of glia nuclei (rosettes) and numerous "focal" changes in the subcortical white substance. Alzheimer was at a loss to classify the condition, which he says was unlike anything so far described. He was inclined to consider it as an atypical Wilson's disease.

A number of other cases are reported which most likely belong with the foregoing types, that is to say, in which the degenerative phenomena predominated. Unfortunately, the microscopic descriptions are so indefinite and inconclusive that these cases cannot be used.

Even in the cases quoted, the histopathologic studies, except those of Alzheimer, are rather superficial and confined to the foci. The remainder of the brain was either neglected altogether or studied partially. It is therefore impossible to ascertain whether the focal lesions were associated with a diffuse process observed in our case.

On the other hand, a few cases have been described in which the morbid process was diffuse only and resembled that found in the cortex and the basal ganglions in our case. Here belong the cases of Creutzfeldt,[8] Jacob[9] and Economo-Schilder,[10] though the last one presents somewhat different aspects. The principal microscopic findings in these excellently studied cases were:

1. Ganglion cell degeneration with accumulation of lipoids.
2. Foci of glia cells with rosette formation.
3. Presence of lipoids in the perivascular spaces of the blood vessels.
4. Foci of destruction in the cortical layers.
5. Hypertrophied glia nuclei.
6. Total absence of inflammatory phenomena, with the occasional presence of rod cells (Stäbchenzellen).

While Economo and Schilder consider their case one of pseudosclerosis, Creutzfeldt and Jacob consider their own cases and that of Alzheimer as instances of a peculiar pathologic entity not previously described. Jacob even attempted to construct a separate clinical syndrome in accordance with the pathologic findings. Though it might be expected that diffuse, like focal, brain degenerations should give more or less characteristic clinical pictures, they must of necessity be exceedingly polymorphous and indefinite. Much will depend on the number of foci, their size and location. The morbid process, for instance, may principally affect either the medulla, pons and midbrain (as in our case), or the large ganglions (as in Alzheimer's case) and give corresponding more or less characteristic symptoms. In addition, the clinical picture will be influenced by the extent of the associated diffuse lesions.

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8. Creutzfeldt, G.: Ueber eine eigenartige herdförmige Erkrankung des Zentralnervensystems, Ztschr. f. d. gesam. Neurol. u. Psychiat. **57**:1, 1920.

9. Jacob, A.: Ueber eigenartige Erkrankungen des Zentralnervensystems mit bemerkenswertem anatomischen Befund, Ztschr. f. d. ges. Neurol. u. Psychiat. **64**:147, 1921; Med. Klinik., 1921, No. 13 (4th case).

10. Economo, C., and Schilder, P.: Eine der Pseudosclerose nahestehende Erkrankung im Praesinium, Ztschr. f. d. gesam. Neurol. u. Psychiat. **55**:1, 1920.

This remarkable association of focal and diffuse degenerative lesions is analagous to phenomena observed in certain inflammatory disorders. Thus in epidemic encephalitis a focal midbrain inflammation is associated with more or less diffuse inflammatory phenomena, while in the present case a focal midbrain degeneration is associated with diffuse degenerative changes. The latter may coexist with slight inflammatory phenomena which, however, in our case, were so indefinite and so uncertain that they may be entirely disregarded. At any rate, it would be illogical to consider the case one of inflammation, in the presence of such intensive and extensive signs of degeneration. While resembling histologically such clinically well defined chronic degenerative diseases as the lenticular degeneration of Wilson, combined cord degeneration, amyotrophic lateral sclerosis, multiple sclerosis and similar essentially *chronic* states, the group under discussion comprises essentially *acute* degenerative states in which the clinical features are obscure, variable and difficult of interpretation.

It is therefore highly probable that, as noted, some indefinite clinical syndromes recorded as acute or "malignant" multiple sclerosis, degenerative encephalitis and disseminated encephalomyelitis, form a separate morbid entity.

For this the name "multiple degenerative softening" would seem to be the most suitable.

## CONCLUSIONS

1. Besides a vast group of acute inflammatory brain lesions, there is an equally large group of acute degenerative brain lesions.

2. The latter present most varied and indefinite clinical syndromes variously described as acute multiple sclerosis, malignant multiple sclerosis, degenerative encephalitis, etc.

3. The inflammatory and the degenerative types resemble one another in the localization of the morbid process, some portions of the brain being affected more, others less.

4. The most conspicuous pathologic features of the acute degenerative type are soft patches which grossly resemble the firm patches of multiple sclerosis, but which microscopically have a definitely different structure.

5. The soft patches are associated with a diffuse degeneration of the brain substance.

6. In view of the specificity of the histologic features of the patches it would be proper to collect the acute degenerative states into a separate morbid group, under the name of "multiple degenerative softening."

# THE MENTAL SYMPTOMS OF MULTIPLE SCLEROSIS *

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NEW YORK

The mental symptoms of multiple sclerosis are of several types, and different writers stress different symptoms. Some describe the euphoric cases, others cases accompanied by dementia, while still others center their attention on the occasional episodes of depression, the delusions and hallucinations. A cursory view of the subject shows that in multiple sclerosis there is not a consistent group of symptoms.

We are quite unprepared to state the incidence of mental symptoms in multiple sclerosis. However, including euphoria, probably in 90 per cent. of cases there are mental alterations which warrant the term "mental symptoms." Because they are overshadowed by physical symptoms and are so often of a character to introduce no element of alarm, they are frequently disregarded. Then, too, the physical condition makes the patient inapt in all his physical undertakings and renders him psychiatrically nonpotential, even in those instances in which unhampered psychotic tendencies would otherwise bring different results. Generally speaking, the patient with multiple sclerosis cannot carry out the things which might lead to committment. Hence it is not surprising that there were only three cases of multiple sclerosis among the 6,700 insane patients in the Manhattan State Hospital.

We have not been able to demonstrate any predisposition to mental disease in these patients; the mental symptoms seem more dependent on the organic brain disease than on an underlying tendency.

## EUPHORIA

Many patients with multiple sclerosis have a slight elevation of mood which may be termed euphoria. Although suffering from a serious disease, they do not think of their condition as serious, nor do they seem deeply concerned about it. In the great majority of cases it does not amount to a psychosis; it is simply a marked inconsistency between the patient's mood and his physical disability. The following case is illustrative:

A woman, 31 years of age, has had symptoms of multiple sclerosis for over ten years and has been in the Montefiore Home for three years. The case is an advanced one. She cannot walk; is nearly blind; her speech is so indistinct that she can scarcely make herself understood; she is so ataxic that she has

* Read before the Association for Research in Nervous and Mental Diseases, Dec. 29, 1921.

to be fed. Despite the almost complete helplessness, she is optimistic and cheerful, laughs and jokes about her symptoms and is not in the least concerned about her condition. Neither is she demented. She can give a full and accurate account of her past life. This euphoria is the only mental symptom.

If euphoria were seen in only one case it might be regarded as individual, depending on the personality of the patient. But it is so frequent that it must be regarded as a mental change associated with multiple sclerosis. It was seen in ten of the fourteen patients showing mental symptoms whom we examined. The euphoria may become much more marked; a manic-like state may result.

Patients in a few cases described in the literature had delusions of grandeur similar to those seen in patients with paresis. This generally occurs as a terminal state associated with considerable dementia. But even these terminal cases do not, as a rule, show the silly euphoria nor the marked change in personality of the paretic. The cause of the euphoric state in multiple sclerosis is not known. The euphoria of paresis and the facetiousness often noted in brain tumor are also not clearly explained.

### STATES OF MENTAL DEPRESSION

Patients with multiple sclerosis have developed suicidal ideas and have attempted suicide. We give an illustrative case:

In a man, aged 28, symptoms were noted four years ago. When he became incapacitated because of his disease he became depressed and attempted to commit suicide with a razor. He was sent to Bellevue Hospital and then to Ward's Island, where he gradually grew worse and was tube-fed over a long period. He attacked other patients without provocation. At present he is irritable, but has grown somewhat euphoric. Although bedridden he thinks he could earn his own way if he left the hospital. His judgment is very poor, but no defects of memory can be determined.

This depressed type of mental disturbance is occasionally seen in multiple sclerosis, but in our experience it is not accompanied by great slowing or retardation. It is probably a mental reaction to the serious condition in which patients find themselves; but even in these cases euphoria tends to develop as the disease progresses.

### MENTAL DETERIORATION

It might be expected that in a progressive organic brain disease such as multiple sclerosis, marked mental deterioration would occur in all patients. This is not the case. Often even in advanced cases, changes of this character are slight or amount only to a chronic mental tension defect. On the other hand, occasionally serious deterioration is seen.

A patient in the Manhattan State Hospital is feeble, partially bedridden, and has greatly impaired vision. His memory is defective. Although he sees the physician from time to time he never recognizes him as the same man and once he thought that the physician was a relative. He cannot distinguish dinner from supper or recall when he has had his meals and when he has not. His judgment is very poor, and he says that he is staying in the hospital to kill time. His mood is one of unnatural complacency. Before he was committed to the hospital he spoke of hearing women's voices talking to him on the street. He imagined that there was some plot against him though he was not insistent about it and when mental deterioration began this trend disappeared.

His family history is so remarkable and so unlike that usually found in multiple sclerosis that it needs special comment. His brother died at the age of 31 of multiple sclerosis with mental symptoms. The diagnosis was confirmed at necropsy. His sister is now in the Central Islip State Hospital, with a case diagnosed as multiple sclerosis, and she also has a psychosis.

Deterioration, in brief, may or may not occur, though probably it is present in a majority of all cases; its degree of progress varies in different patients, only occasionally becoming profound; and as would be expected, as it develops it obliterates, to a large degree, tendencies which may have been present. Some patients have only a mild disturbance of memory, of which they are entirely aware. In a few reported cases there have been Korsakoff-like pictures, but we have found no such cases and feel that this type is rare.

### HALLUCINATIONS

Auditory hallucinations without insight and occurring as a feature of a delusional trend are not unusual. The case mentioned in the foregoing is a typical instance of this.

We have to report a single example of considerably more bizarre hallucinatory phenomena in a case observed at the Neurological Institute:

A young woman, 31 years of age, whose physical symptoms have existed for two and one-half years, for many months has had visual hallucinations: To her the rug appears to be on fire and smoke issues from the carpet. She has seemed to see bright green beetles crawling on the window-pane. Occasionally she has seen people approach the door and she has not known definitely, until reassured, that no one was there. The remarkable feature is that she has perfect insight into these experiences. She cannot be said to be suffering from a psychosis, and she realizes that these false impressions are caused by her disease.

On one or two occasions she has had hallucinations of hearing, such as a band playing or voices singing. There are no hallucinations of taste, touch or smell. Examination of the eyes revealed 20/50 vision in the right eye; 20/70 in the left eye, with temporal pallor of the optic disks and some contraction of the visual fields.

The character of the hallucinations suggests that they arise on some irritative or toxic basis either in the higher visual centers or in the pathways leading to them.

### TRENDS

Cases are occasionally seen which bear a certain resemblance to dementia praecox, of which the following is an example:

In a woman, aged 35 years, severe mental symptoms began after the disease had existed for nine years. Although she was entirely blind at that time, she thought that people were watching her, that they came into her room at night, and that they were threatening to kill her. She spoke of hearing voices. Much of her thought content had to do with sex affairs. She thought that men were paying her attention with the idea of marriage.

Although bedridden and entirely helpless she still talks about the possibility of marriage. However, these paranoid trends have almost entirely disappeared, and now she is mildly euphoric or at least contented and happy.

In this case the delusional trend and hallucinations may be less directly dependent on an organic lesion and appear to be of a more dementia-praecox-like nature. In none of our cases have we found negativistic phenomena or catatonic reactions.

### PERSONALITY

Apart from certain mood changes, for example euphoria, patients with multiple sclerosis usually retain the same personality that they had before their illness. Even though there is deterioration, they do not as a rule show marked moral and ethical changes, and there is comparatively little of the grave disturbance of personality common in paresis. In this domain it is reported that those cases have resembled paresis most which at necropsy showed considerable lesions of the frontal lobes. However, even in such cases, personality changes were not great.

Careless use of terms has led some writers to talk of hysterical and neurasthenic reactions in the disease. We are struck by the absence of such features in the cases which we have studied.

### COURSE OF MENTAL SYMPTOMS

An interesting characteristic of the mental symptoms in multiple sclerosis is their marked tendency toward change and tendency toward regression of certain of the phases, particularly the trends. Often the paranoid and delusional states are of only a few months' duration. The brevity of these states may be quite unexplainable. They may disappear as deterioration advances. With the subsidence of trends, there is a tendency for euphoria to increase, and grandiose elaboration may be a very late development.

## CONCLUSIONS

Our observations lead us to divide the mental symptoms of multiple sclerosis into two groups: first, those which are primary and directly the result of the organic lesions; second, those which are incidental and secondary.

In the first group we would place euphoria, since it seems to be associated with the organic brain condition; likewise the mental defect symptoms, the occasional hallucinations of organic origin and the very rare confused states and Korsakoff's psychosis; also the occasional terminal states with delusions of grandeur.

In the second group we would place those transitory delusional states and depressions which appear to arise as a result of the condition of incapacity in which the patient finds himself. Here probably belong suicidal attempts and delusional trends accompanied by hallucinations often of only a few months' duration. There are still other delusional trends which are more like dementia praecox. However, marked distortion of thought and oddities of conduct which are so frequent in dementia praecox are not encountered in multiple sclerosis.

While multiple sclerosis has symptoms in common with other organic brain diseases, the mental symptoms do not closely resemble these conditions. The clinical picture is not that of paresis nor that of cerebral arteriosclerosis. The symptoms are more like those occasionally seen in brain tumor.

There is no correlation between the parts of the body showing the effects of the disease in greatest intensity and the content of delusional or hallucinatory trends.

It is reasonable to suppose that the secondary symptoms, such as depressed and paranoid states, depend to a considerable extent on the mental makeup of the patient before the disease developed; but with the primary mental symptoms of the disease this is not the case. Although the latter are quite variable, they are not more so than are the physical symptoms.

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# Abstracts from Current Literature

THREE CASES OF TUBERCULOUS MENINGITIS RESEMBLING EPIDEMIC CEREBROSPINAL MENINGITIS; RACHIDIAN POLYNUCLEOSIS. Riser and Roguer, Ann. de méd. **10**:10 (July) 1921.

This is a comprehensive article dealing with a comparatively uncommon clinical variety of meningeal tuberculosis, and the writers cite three illustrative cases.

In the course of tuberculous meningitis without superimposed infection, polynucleosis in the spinal fluid is not exceptional. This polynucleosis may be caused by an abundance of organisms, the nearby presence of an old caseous meningeal focus, or subacute evolution. But each of these causes taken alone cannot explain all the cases, and the pathogeny of the reaction is still not entirely established.

Bearing on this point, however, the writers report their own experiment in which they have injected tuberculous toxins, isolated by the D'Auclair method, in the subarachnoid space. One injection brought about a polynucleosis lasting from four to six days and repeated doses, at intervals, induced a permanent reaction. They then suggest that in tuberculous meningitis the spinal fluid polynucleosis may be due to the repeated liberations of toxins in the subarachnoid cavity.

The authors say that in the presence of a polynucleosis, without proof of the presence of the micro-organisms of an acute infection, the Koch bacilli should be searched for. In all doubtful cases antimeningococci serum should be injected because it is beneficial in epidemic meningitis and does not aggravate the prognosis in tuberculous meningitis.

SOME DETAILS OF TECHNIC IN SPINAL ANESTHESIA. Rene Dumas, Bull. Med. **36**:22 (Jan. 11) 1922.

This is an interesting defense of spinal anesthesia which, in the opinion of the author, has been left in comparative disrepute, chiefly owing to the omission of certain features of its proper administration.

A preliminary injection (subcutaneous) of morphin is indispensable (1 to 2 cg.) and should be given 45 minutes prior to the lumbar puncture. At the same time that the morphin is injected, the writer advocates the injection of 1 to 2 mg. of strychnin and 5 cg. of spartein. These drugs combat the onset of symptoms due either to bulbar intoxication or anemia.

For gastric surgery, the lumbar puncture and injection is given between the first and second lumbar vertebrae, for pelvic, between the second and third and for perineal between the third and fourth. If one makes the puncture between the first and second lumbar vertebrae, it is necessary to be careful not to prick the conus. It is probable that some of the reported cases of sphincter incontinence are due to such injury.

Remove 25 c.c. of spinal fluid or more, even 30 or 40 c.c. if that is necessary to reduce the flow of fluid to a slow drop by drop flow. It is well to draw off fluid to this extent because the subsequent diffusion of the analgesic liquid is thereby favored.

Cocain when injected gives a rapid and sure anesthesia but is "brutal" and should seldom be employed. Stovain, less toxic, gives a good anesthesia, but has not been proved that it does not effect an irritation of the pia mater and nerve cells. Procain is best, inasmuch as its action is rapid and toxicity feeble. The dose varies with the desired duration of anesthesia. The writer finds that 12 cg. of procain gives an hour of anesthesia for the entire abdomen. Eight centigrams suffice for the current operative procedures of pelvic surgery, with about 45 minutes of anesthesia. Five centigrams, for the anus and perineum, give the same duration.

The writer emphasizes the great importance of pure and properly sterilized drugs for the purpose.

Of the accidents of the procedure, retention of urine occurs in from 10 to 15 per cent. of the cases of abdominal intervention—the large dosage employed? It lasts from one to six days. Meningeal signs are exceptional and are treated by repeated lumbar punctures.

The principal contraindications for this method of anesthesia are all conditions of shock and of infection—such conditions as intestinal occlusion, strangulated hernia, peritonitis and grave hemorrhage. On the other hand, apart from shock and infection, "pelvic surgery is the triumph of spinal anaesthesia."

RADICULAR SCIATICA WITH REFLEX GLYCOSURIA AND SYMPATHETIC DISORDERS IN A TUBERCULOUS PERSON. NECROPSY CYST ON A LUMBAR ROOT. RADICULO-SYMPATHIC REFLEXES. LORTAT-JACOB, Progrès méd. **36**:611 (Dec. 31) 1921.

This report concerns a case of advanced pulmonary tuberculosis in which severe unilateral root symptoms localized in the right leg complicated the clinical situation. For the last two years of life there were recurring sciatic attacks. During the late and severe recrudescences, there were striking vasomotor signs in addition to the absence of the right ankle reflex, muscular atrophy of the muscles supplied by the fourth lumbar root, anesthesia in the same radicular zone, and excruciating causalgic radicular pains with diffuse hyperesthesia. The clinical picture was further complicated by a glycosuria which the writer calls a reflex glycosuria "analogous to that which one obtains by irritation of the central end of the sciatic nerve." Under the influence of sedative treatments, including the epidural injection of procain on two occasions, the glycosuria disappeared, and this is considered further evidence of the reflex pathogeny of the metabolic disturbance.

Necropsy revealed, besides the expected lung lesions, a transparent cystic proliferation on the right fourth lumbar root.

DAVIS, New York.

LATE THERAPY OF NERVE WOUNDS. THEODOR MAUSS, Ztschr. f. d. ges. Neurol. u. Psychiat. **65**:36, 1921.

The treatment of old nerve injuries, Mauss considers under two heads: operations on the nerves themselves, and orthopedic measures. His article is full and well balanced, and summarizes the experience of German workers during the seven years since the beginning of the World War. There is nothing strikingly original reported; methods and statistics are to be found in articles by Foerster, Krueger, Stoffel and others. This is a general review of the situation. The most striking statements are those concerned with the time required for the regeneration of nerves.

The author devotes a few pages to the manifestations and theories of degeneration and regeneration, and gives these practical conclusions:

1. Regeneration of nerves is impossible unless the severed ends are joined.

2. Healing by primary intention with immediate return of function is impossible.

3. Possibility of regeneration is always present although in the course of years it becomes diminished. "We do not know 'too late' in nerve operations."

With these principles in mind, Mauss says that every patient with a severe lesion should be operated on.

Beginning with the simpler operations on nerves, the author believes that when the nerve is intact, surgical procedure should depend on the density of the scar, the ease with which the nerve is separated into fasciculi either by hand or by intraneural injection of saline, and the effect of direct faradic stimulation. Perineural and endoneural neurolysis are recommended when conditions are satisfactory.

In complete division direct suture is the simplest and most satisfactory measure. In some cases this is easy, but when the defect is large, direct suture may be accomplished only by stretching, mobilization of the nerve, transplantation from extensor to flexor surfaces, or tunneling. The ends must be absolutely healthy and must not be too much compressed by scar tissue.

When direct suture cannot be performed some other method must be employed, such as nerve grafting, nerve muscle implantation, free transplantation, bridging or interposition of physiologic tubing. Grafting is suitable when nerves are sufficiently near one another. Nerve muscle implantation has been fairly successful in the hands of Foerster and Borchard. Free transplantation has been successful only with autoplastic grafts. Bridging takes considerable time for regeneration and is not very satisfactory. Interposition is least useful because naked axis cylinders can travel but 2 cm. at most.

When should a secondary operation be considered? The most recent work shows that far more time is required for regeneration than was supposed. After suture, some improvement is usually noted in from three months to two and one-half years in the arm, and even after three years in the leg. Excluding the possibility of technical defects in the operation, it is wise to postpone secondary operation for three or even four years. After grafting, musculoneurotization and free plastic, results are less certain, but according to Foerster results should be expected in from four to six months.

In estimating return of function in paralyzed muscles we must exclude compensating mechanisms, such as substituted movements, apparent movements and vicarious intrusion of foreign nerves either by anastomosis or by extension. This is common in sensory nerves but rare in motor nerves. After some recovery of function, secondary operation should be undertaken when improvement has definitely ceased.

Signs of returning function are first a sharper contraction to the galvanic current, then voluntary movements, and finally faradic excitability. Sensation is less valuable than electrical excitability, principally because of penetration of foreign nerve fibers into the anesthetic field. Valuable signs, however, are improved vasomotor and secretory conditions. Tinel's sign is not mentioned by the author.

When improvement under nerve operations ceases, orthopedic measures are in order, principally tenodesis, or shortening of tendons, and tendon transplantation. On account of the fixation necessary and frequent rigidity resulting, the former procedure is not often used. Tendon operations should not be

undertaken until all hope of recovery of nervous function is abandoned. These are the indications given for primary tendon operations: (1) intractable fistulae; (2) extensive scars, dense, and reaching to the bone; (3) severe damage to muscles supplied by the nerve; (4) unfavorable anatomic conditions, such as damage to the nerve shortly before branching or departure from the parent trunk; (5) evident latent infection; (6) excessive nerve defects; and (7) previously operated cases that have been unsuccessful and give no hope from repeated operation on the nerve.

Mauss lays special emphasis on the necessity for waiting sufficiently long after the primary operation before considering secondary operations or orthopedic procedures, and he gives instances in which in view of the long time required, these secondary operations were undertaken, and later evident power returned in the distribution of the nerve first operated on. The same objection holds for appliances. They postpone attempts to use the part and also tend to increase the fixation of the limb and to interfere with the proper circulation. Especially will these appliances give rise to habitual paralyses, even after electrical reactions are normal. Of course in peroneal palsy a brace is necessary to maintain the limb in good position, but in all cases systematic attention should be given to massage, passive and active movements, hydrotherapy and electricity.

Physical therapy is especially indicated in conditions of vasomotor and trophic disturbances in order to avoid alteration in the bony structures and contractures of the muscles. They are necessary above all in plexus injuries.

The author devotes a few pages to the discussion of irritative phenomena in sensory nerves, the so-called wound neuralgias. They are marked by hyperexcitability of sensory nerves and are located principally in the distal portion of the extremity. They are most common in injuries to plexuses, and the median, ulnar and tibial nerves. The anatomic substrates in these cases are most often strangulation, endoneural scars, and foreign bodies, especially bits of cloth. The combination of trauma and infection sets up neuritis which is very troublesome and persistent. The severe cases demand early operation. The best results are obtained by releasing the nerve from the scar tissue, or neuraxiresis. Foerster recommends resection of the damaged portion and suture in severe cases. Another method is freezing by ethyl chlorid, which must be thorough and deep in order to penetrate the nerve and induce lasting effects.

UNIVERSAL INFANTILE DYSTROPHY. S. Hirsch, Ztschr. f. d. ges. Neurol. u. Psychiat. **72**:347, 1921.

Hirsch blames "der Blockade" (the blockade) for the recent increase of infantilism. His twelve patients during the period of adolescence lived under unhygienic conditions, nine being orphans, and most of them suffering more or less from chronic malnutrition. This exogenous factor has been emphasized by Anton, but the pathogenesis Hirsch ascribes to endocrine disturbances. The individuals at the age of 18 to 23 are of short stature and childish physique. Their long bones are open at the epiphyses and in many cases there are signs of rachitis tarda. The changes are not only in the bones, however. Five of the twelve had genitalia of infant size. All of them lacked secondary sexual characteristics, such as hair growth, deepening of the voice, libido, control of the emotions and interest in manly occupations. Most of them had hyperplasia of the lymphoid structures, some were asthmatic, others showed signs of hyperactivity of the vegetative nervous system, all of them showed diminished thyroid function, and some the symptoms of hypopituitarism.

Hirsch believes that enforced poor hygiene such as prevailed during the war, especially in these cases, caused grave endocrine disturbances at that important developmental period, adolescence.

ETIOLOGY OF TABETIC ARTHROPATHIES. KURT GRASSHEIM, Ztschr. f. d. ges. Neurol. u. Psychiat. **72**:119, 1921.

Before advancing his own theory as to the etiology of tabetic arthropathies and pathologic fractures, Grassheim discusses the theories that have been advanced at one time or another to explain these manifestations, about fourteen in number. The most important ones are: (1) degeneration of trophic centers in the spinal cord, (2) trophoneurosis, (3) ascending neuritis, and (4) trauma to tissues undefended by normal reactions to pain.

The frequent occurrence of bone disease before ataxia and before disturbances of sensation either superficial or deep led him to inquire into the nature of the disorder. Chemically he found diminution of calcium and phosphorus in the bones of tabetic patients, to the extent of 30 per cent. Microscopically, he found local destruction of bone, fissure formation and widening of Haversian canals. Further he states: "It is notable that in spite of the activity of the resorptive process, osteoclasts were present in small numbers so that they cannot be blamed for the disturbance. Callus formation is chiefly fibrous, with inlays of osteoid tissue and new formed bone, but osteoblasts are lacking at the periphery."

No nerve degeneration was found in 550 sections stained by various methods. Treatment by administration of calcium salts and organic phosphorus was unsuccessful in arresting the course of the bone disease.

Grassheim believes that the disturbance is one of bone metabolism, and therefore linked with endocrine disturbances. He calls to mind the frequency of endocrine disorders in tabes (impotence, emaciation, glycosuria, etc., together with other less frequent but well-known pituitary and thyroid disorders), and places tabetic arthropathies in this category. His article is extensive and well written, but is a comment on our ignorance of bone metabolism, and especially its relation to endocrine disorders.

FREEMAN, Philadelphia.

EXPERIMENTAL DEGENERATION OF THE VAGUS NERVE AND ITS RELATION TO THE NERVE TERMINATIONS IN THE LUNG OF THE RABBIT. O. LARSELL and M. L. MASON, J. Comp. Neurol. **33**: 509-516 (Dec. 15) 1921.

The vagus nerves supply the preganglionic fibers to the intrapulmonary ganglion cells which are scattered along the bronchi and their branches, as is shown by the disappearance of most of the pericellular networks about these cells following experimental degeneration of the vagus of the same side. Most of these preganglionic fibers come from the vagus of the same side, but some from the vagus of the opposite side. The number of fibers in the bronchial musculature is affected very little, if at all, by the degeneration of the fibers of the vagus nerve. These are, therefore, postganglionic fibers arising probably from cells of the intrapulmonary sympathetic ganglions. A few sensory terminations remain in the lung of the operated side after degeneration of the vagus fibers; these are believed to be derived, in part, from the vagus of the opposite side. The number of nerve fibers in the walls of the pulmonary blood vessels is unaffected by degeneration of the vagus nerve.

THE GROWTH OF THE CENTRAL NERVOUS SYSTEM IN THE HUMAN FETUS AS EXPRESSED BY GRAPHIC ANALYSIS AND EMPIRICAL FORMULAE. HALBERT L. DUNN, J. Comp. Neurol. **33**: 405-491 (Dec. 15) 1921.

This is an exhaustive statistical study of 156 human fetuses ranging in length from 3.1 cm. to 53.6 cm. The growth of the central nervous system throughout the fetal period is similar to the growth in body weight at this time. The growth of the central nervous system, on further analysis, shows three distinct subtypes: (1) cerebral growth, which is slow and steady prior to the sixth fetal month (30 cm.) and is more rapid from that time to birth; (2) brain stem and cord growth, which is more rapid from the second to the last of the fifth fetal month than it is thereafter, and (3) cerebellum growth, which is very slow from the second to the last of the sixth fetal month and extremely rapid in the last four months of intra-uterine life.

VERTEBRATE CEPHALOGENESIS. V. ORIGIN OF JAW APPARATUS AND TRIGEMINUS COMPLEX—AMPHIOXUS, AMMOCOETES, BDELLOSTOMA, CALLORHYNCHUS. HOWARD AYERS, J. Comp. Neurol. **33**:339-404, 1921.

A detailed comparative anatomic study of the species named in the title leads the author to the conclusion that the evolution of the jaw apparatus is not related to that of the gills, as commonly taught. The mandibles are derived from the cirri or tenacular apparatus of *Amphioxus*. The maxillary structures arose later within the cyclostomes. The history of these transformations is outlined and supported by a detailed examination of skeleton, muscles and nerves.

STUDIES ON THE RETINA. HISTOGENESIS OF THE VISUAL CELLS IN AMBLYSTOMA. S. R. DETWILER and HENRY LAURENS, J. Comp. Neurol. **33**:483-508 (Dec. 15) 1921.

The fully differentiated retina of amblystoma punctatum possesses characteristic rods and cones. In early stages of development the visual cells are all conelike. Rods do not appear in their definite form until relatively late in development. Rods, however, do not differentiate from cones, but at very early stages the conelike elements are of two kinds (present in the ratio of 4:3), which give rise, respectively, to definitive rods and cones.

C. J. HERRICK, Chicago.

THE VALUE OF PHENOBARBITAL (LUMINAL) IN THE TREATMENT OF EPILEPSY. L. CHEINISSE, Presse méd. **30**:42 (Jan. 14) 1922.

This critical review calls attention to the limitations of phenobarbital (gardénal). There was no effect in some cases of grand mal; debatable effect in petit mal—the writer concludes that some benefit may be expected; rash and sore throat were reported in a few cases; there is danger of status epilepticus when the drug is suddenly interrupted; incidence of intellectual torpor is frequent and there is occasional delirium. Some injury to intellectual activity is almost constant.

The writer comments favorably on the suggestion of M. Ducosté (Note complémentaire sur le traitement de l'épilepsie par la phényléthylmalonylurée,

*Ann. méd. psychol.*, July, 1921) that belladonna in small doses can be used with luminal to improve the psychic condition and correct the constipation, together with very small doses of caffein to combat the mental and physical lassitude.

PERIODIC OCULOMOTOR PARALYSIS DURING RELAPSING FEVER. T. MIRONESCO, Presse méd. **30**:17 (Jan. 7) 1922.

The author reports a case of oculomotor paralysis on one side, which appeared during an initial attack of relapsing fever, disappeared entirely during remissions, and recurred in its original form during two successive relapses. The attacks of paralysis coincided with the finding of spirilla (Obermeyer's) in the circulating blood. This repeated constant localization was thought to be due to spirilla in the capillaries with a local predisposition, possibly a small hemorrhage. The spirilla were not found in the cerebrospinal fluid in this case, but have often been reported there before, even anticipating the appearance of an initial attack of fever. Hemorrhages have also been described in the meninges in other cases. Attention is called to the importance of these observations now that cases of general paresis are being treated by inoculation of relapsing fever. Eye muscle palsies may be due to complications of the two diseases.

SYRINGOMYELIA WITH SPINA BIFIDA. M. KLIPPEL and A. FEIL, Presse méd. **29**:971 (Dec. 7) 1921.

This case, with necropsy findings, is claimed to be the first of the kind reported in an adult. It is argued that there is some connection between the two malformations, that the syringomyelia in this case was congenital, and that the same cause produced both abnormalities. The two types of lesions, syringomyelia and spina bifida, generally appear to be independent but in this instance they occurred in the same case and constitute a new syndrome of "ependymal-arachnoid hydromyelia."

HUDDLESON, New York.

APHASIA. M. CHRISTIN, Rev. méd de la Suisse Romande **41**:717-727 (Nov.) 1921.

Since the celebrated discussion of the Neurological Society of Paris, in 1908, little advance has been made in the study of aphasia.

Monakow has pointed out the error that has been made in confusing the localization of aphasia with the localization of language. How severe a lesion is required to produce an aphasia remains doubtful. It is necessary for the anatomist to take into account initial phenomena, residual states, functional elements and bilateral compensation before the anatomic site can be postulated in the various syndromes.

During the past year Head has reviewed the ideas of Jackson (*Brain* **43**: Pts. 2 and 4, 1920). Head's conception of aphasia is psychologic, not based on anatomic verification. In the study of his patients he used methods which are very extensive. His scheme tends to show that identical stimulation may provoke various responses; however, his results are not always conclusive. The method of examination as employed by Head is explained by the writer in full. A series of his tests deal with recognition, imitation, description, calculation and various other phases, as employed in the usual aphasic examination. In studying a large group of aphasias occurring among soldiers, Head thought it possible to abandon the traditional conception of localization. He

considers language difficulties as complex even in the more simple anarthrias or motor aphasia. In motor aphasia there is always some alteration of internal language. Head agrees with Marie that in aphasia all parts of speech are affected but in variable proportions. Verbal images are not entirely lost, as the words may reappear under suitable stimulation, even though they cannot be returned at will. It is this phenomena that Monakow, following the terminology of Semon, calls the failure to exphoriate the engrammes.

In aphasia recognition is usually possible as patients demonstrate by gesture that an object or picture is recognized, but there is an inability to get the corresponding word. Words may even be recognized, but they do not evoke the corresponding image or object. The same is true in dealing with a foreign language; there is a suspicion that a word is known, but the meaning fails to present itself. This Head calls symbolic thinking, which is the use of symbols for objects or conceptions. Marie does not believe that we think in terms of words but that all internal reflection occurs in phrases. Many simple acts are executed without presenting themselves verbally. In Head's classification of the aphasias he takes into consideration residuals. There are verbal aphasias, nominal aphasias, syntactic aphasias, semantic or coordination aphasias. The first two types agree fairly well with motor and sensory aphasias. The latter two groups are entirely new and originated by Head. He looks on aphasia as a syndrome which varies only in proportion to divers elements which compose it. He does not believe that a purely motor, visual, auditory or verbal aphasia occurs. The aphasic person has great difficulty in thinking out a problem. Voluntary language suffers more than the automatic or emotional, and often the patient who is unable to repeat a phrase is able, under emotion, to speak it correctly.

Numerous objections have been made by English neurologists to Head's views. Collier leans to the exact anatomic localization of the psychic functions. Stewart also remains true to the classic localization and reports cases following war injuries to illustrate his contention. Unfortunately he has no anatomic proof. Wilson believes that Head's tests are more intellectual than aphasic. He does not see how his tests of imitation show defects in internal verbalization. Wilson agrees with Monakow. He believes that verbal images are perhaps conservers in the form of engrammes without which their voluntary evocation is impossible. Wilson tends to accept Déjerine's classification, and he believes that Head's groups are not clear cut. Stanley Barnes tends to accept Marie's teachings in that he believes intellectual function is internally bound to language.

Before passing judgment the author believes it is well to await the anatomic verification of Head's cases. It does not suffice to deny the localization theory and the work of anatomic clinicians. It is well to compare by analogy this complex speech mechanism which is put into play by language. The author compares the aphasias as follows: A lesion of the third or sixth nerve or nucleus gives a condition analogous to an anarthria. Alteration of the optic nerve, eighth nerve or their nuclei represents the visual or auditory aphasias. Lateral movements of the head and eyes are more complicated, and it is necessary to postulate a lesion of the reticular formation, the posterior longitudinal bundle and of the island of Reil. As the movements get more complicated more of the brain is involved, and the analogy of a sensory aphasia is produced. We therefore may look on speech as a refined motor reflex. In primitive people the response to external stimuli is globule. For good understanding gestures must be relied on, and only with time does the word detach itself from the thing

which it represents. Thus from a verbal image it becomes a symbol. The development of language goes on apace with the increase of intelligence and the needs of the person. It is well known that the cortex has the function of differentiation and of discrimination, while the basal nuclei are characterized by a more diffuse reaction. In the psychic sphere it may be said that the basal nuclei have a marked instinctive character, while the intelligence, the faculties of discrimination, are cortical in origin.

According to Monakow's theory of diaschisis, sudden lesions carry with them many associated symptoms. These gradually clear away. Slowly developing lesions, on the other hand, may continue for a long time without any associated symptoms. In the formation of language a great extent of the cortex is activated. The various centers, such as Broca's and Marie's, are only stations at which fibers condense and by injury produce definite isolated disturbance of function, but not wholly attributed to the injury itself. To understand the production, the continuation or regression of an aphasia, it is necessary, following the teachings of Monakow, to study not only the localization of the lesion, but also the nature of the pathologic process, the condition of the brain prior to the trouble, the toxic influences, the disposition of the patient and the means by which language has been acquired.

Language, which is the general mode of expression, is as the white light in the solar spectrum; it is the resultant of all the radiations, localized in one part.

DIAGNOSIS AND TREATMENT OF CORD TUMORS. Emil Redlich, Med. Klin. **17**:1315 (Oct. 30) 1921.

The treatment of cord tumors presents one of the bright chapters in neurology. Horsley, in 1887, was the first to remove a cord tumor. This had been diagnosed by Gowers, and the operation resulted in complete recovery. Since Horsley's work, rapid strides have been made both in the diagnosis and treatment of cord tumors. Today an exploratory laminectomy is looked on as a harmless procedure and frequently establishes an otherwise uncertain diagnosis.

Under the heading of cord tumors, growths arising from the roots and membranes, tumors of the vertebra and also extravertebral tumors must be considered, as they may have to be considered in the differential diagnosis.

Intravertebral tumors may be divided into extradural and intradural growths. The intradural tumors, which are the most important, are divided into extramedullary and intramedullary tumors. It is rare for the dural tumor to extend into the cord. It is just as rare for the medullary tumors to extend into the membranes or into the roots. It is possible, as has occurred in the author's experience, to have two types of tumor in the same patient.

According to Schlessinger, vertebral tumors are more frequent than intramedullary tumors, in a ratio of about two to one. The author believes that this proportion is perhaps too high, and is due to the large amount of postmortem material which Schlessinger had to deal with. Intramedullary and extramedullary tumors, according to the same authority, occur with equal frequency. Oppenheim and others find the extramedullary type more frequent, about three to one.

The dorsal region is the most common location for extramedullary tumors, next the cervical, then the lumbar and sacral. Intramedullary tumors are seen most frequently in the cervical and lumbar regions. Extramedullary tumors have a preference for the posterior surface of the cord.

Intradural tumors usually consist of endotheliomas, especially psammoma-endotheliomas, fibromas and varieties of sarcoma, more rarely lymphangiomas, myxomas and lipomas. On the nerve roots, fibroma—especially neurofibroma—is the common type, occasionally multiple as in Recklinghausen's disease. The author has also seen a fibro-endothelioma and teratoma with dermoid cysts, arising from the cauda equina. It is not unusual to have in the cauda equina malignant tumors, such as sarcomas and carcinomas. These are usually metastatic, most frequently from the prostate or mammary gland. Granulomas are not rare, especially tuberculomas.

Endotheliomas and fibromas may arise from the pia. They may penetrate the cord so as to give a picture of an intramedullary tumor. Malignant tumors may also arise in the pia, as sarcoma which may be multiple. The multiple sarcoma may resemble clinically a meningitis, and by preference select the dorsal side of the cord. Tuberculomas, which are usually intramedullary and frequently solitary, occur in the gray substance of the cord. They may be multiple or associated with cerebral lesions in which there is usually a terminal meningitis. Gliomas are usually intramedullary and may present the picture of a syringomyelia. Gliosarcomas are also present, usually grow slowly, and may become very extensive. Sarcomas may present similar conditions. Gummas are rare, and even more infrequent are neuromas and angiomas.

Extradural tumors are usually sarcomas, endotheliomas and lipomas. Metastatic growths are especially common, such as sarcomas and carcinomas. In a case of pachymeningitis tuberculosis externa, reported by Pelz, there was a classical picture of extradural tumor.

Primary tumors of the vertebra are rare. Sarcomas, osteomas and enchondromas occur and may be operable; usually they are multiple. Myelomas occur, but like sarcoma and carcinoma are usually not of therapeutic interest. Echinococcoses are rare; they may grow out toward the skin and present a cystic mass. Tumors on the surface of the dura are the easiest to operate on, then the root tumors, intramedullary and vertebral.

From the standpoint of symptomatology and progress, cord tumors may be divided into extramedullary and intramedullary types. This is not a sharp line and frequently the exact location cannot be definitely determined. In the extramedullary type there is usually a latent period without any or only vague symptoms. The author has on several occasions in traumatic spine injuries discovered dural tumors that had given no symptoms. Following the latent period there is usually a stage of radicular pain when dorsal roots are involved by the pressure or growth. Intercostal neuralgia, girdle pains and paresthesias are among the common complaints. These may fail, however, or appear very late. The entire course may be without pain. Motor irritation symptoms are rather rare, for, as stated, the tumors are usually on the dorsal side of the cord. The progression of symptoms may take various courses. A Brown-Séquard syndrome may occur. It is noted by the author that the marked hyperalgesia on the side of the lesion, which is noted in animal experimentation, is not present in human beings. The Brown-Séquard syndrome, even if not clear cut, may be suggested by the difference on the two sides of motor and sensory involvement. Early progress may be slow. Later it may be rapid and within a short time paraplegia or tetraplegia may occur. An island-like sensory disturbance, gradually extending cephalward or caudalward, may first be noted. More frequently, however, there is an ascending disturbance. The upper limit of anesthesia does not affect the various qualities of sensation in the same

manner. Foerster and the author state that the term anesthesia is the highest involved, next the analgesia and hypalgesia and last the anesthesia and hypesthesia. It is not infrequent in dorsal tumors for the lower sacral segments to remain intact. A marked compression may produce a flaccid paralysis, but the prognosis is not so bad as might be supposed, as even in these cases restitution is possible though more difficult. Bladder disturbances are among the early symptoms; at first there is difficulty in urination with residual urine and later complete retention. A patient with a late case may have incontinence (ischuria paradoxa). Here the cystoscopic examination usually shows a trabeculation of the bladder. In lesions of the cauda or conus which contain the bladder centers, incontinence with cystitis develops early. Besides these cardinal symptoms there are numerous neighboring and distant symptoms, such as pressure signs due to spinal fluid pressure—for example, an ascending anesthesia above the level of the tumor. This may be assumed when in a tumor of the cauda or conus an increase in the leg reflexes occurs, due to pressure on the pyramidal tracts. As distant symptoms one may have, as noted by Cassirer, Foerster and others, the appearance of conus symptoms in dorsal tumors. Nystagmus, abducens and facial palsy have been noted and attributed to this cause. Late in the disease percussion and pressure tenderness may occur. Walking may be painful, it being necessary for the patient to sit up at night. Stiffness of the back, lordosis or kyphosis may occur. Roentgen-ray examination is usually negative.

The clinical picture of a medullary tumor is not as typical as that of an extramedullary tumor. The symptoms tend to be transverse. Gliomas have a tendency to grow lengthwise and may attain considerable size. The symptoms depend very much on the nature of the growth. Gliomas frequently give the picture of a syringomyelia except that the course is usually much more rapid. Atrophy may occur when the lesion is situated in the anterior horns, and only later posterior signs develop. Pains are rather unusual. They may, however, be severe, in which case the picture resembles that of an extramedullary growth.

The author discusses tumors of the vertebra only in so far as they have reference to the spinal cord. It is important to know whether the tumor is primary or secondary. The roentgen-ray is of great help in this connection. The cord symptoms usually appear late, but the onset may be very acute. In this connection caries of the vertebra must be borne in mind, for when caries occurs in the arches the diagnosis is difficult.

The course of tumors of the cord, roots and membranes is usually chronic and progressive. Cases have been reported with a history of ten and twenty-four years, respectively. Occasionally the progress is rapid. Long remissions are not uncommon, especially in intramedullary tumors. In these cases the diagnosis may be doubtful and one necessarily thinks of an arachnitis, which is prone to be more regressive than a tumor. In the differential diagnosis meningitis or arachnitis circumscripta must be considered. Operative measures in these cases produce good results. During the war circumscribed arachnitis was frequently noted. Infections, vertebral tumors, caries, spondylitis deformans, pachymeningitis externa, as also affections of the cord itself, such as multiple sclerosis and funicular myelitis, must be considered. In multiple sclerosis the picture of a transverse myelitis may present itself. On the contrary, nystagmus is not infrequent in dorsal cord tumors, with a loss of abdominal reflexes. Pains also may occur in multiple sclerosis, and even a Brown-Séquard syndrome has been noted.

In recent years the spinal fluid has aided considerably in the diagnosis of cord tumors. While not diagnostic of the various types of tumor, it is especially valuable in distinguishing neoplasms from purely spinal conditions. The compression syndrome of Nonne, which consists of an increase of globulin and albumin and a normal or only slightly increased cell count, is a fairly common finding. Occasionally, however, there is an increased cell count. This usually, but not always, indicates an inflammatory process with compression of the cord, as in caries or pachymeningitis. Xanthrochromia, which is due to a moderate diapedesis, is most frequently found in tumors of the cauda or lower cord, while the simple globulin increase is more frequently found in tumors of the upper cord. Another symptom of spinal fluid interruption is the Queckenstedt phenomena. This is based on the principle of equal distribution of fluid. When a puncture is made and the neck pulled forward, an increase of spinal fluid pressure between 100 and 200 mm. occurs. In tumors this increase, if noted, is slight. On coughing and abdominal compression the pressure will rise, due to the change in the local extradural and intradural venous plexus pressure. In cases of cord tumor there is an interruption of the flow of fluid; thus on puncture there is a sudden gush followed by only a few drops. The compression syndrome and Queckenstedt syndrome tend to blend. The latter gradually evolves during the course of the disease as the author has noted by repeated puncture in the same case. Occasionally in a study of the fluid the author has found tumor cells, also cysts.

The location of the neoplasm is usually determined by the sensory and motor findings. As a rule, only the upper pole is of localizing value, and it is not unusual to find it necessary for the laminectomy to be extended in either direction. The sensory findings are usually much more accurate in localization than motor phenomena. Radicular pains are also of value in the localization. It is well to remember that no segment of the skin or muscle is represented by a single segment in the cord, as there may be over lapping of from two to three segments. In the noted case of Horsley and Gowers the tumor was localized too low because of this fact. It is not infrequent that tumors are localized too high, due to associated swelling, pressure, etc., above the tumor. In dorsal tumors sensory findings are frequently absent and localization is difficult. Foerster has described a special form of tactile disturbance—the recognition of written tactile stimuli on the skin. The author does not consider this of special value.

The relationship of the cord to the vertebral column must also be borne in mind and sufficient room given for this difference in establishing a level. It is also important in dealing with caudal tumors to determine whether the growth is intravertebral or extravertebral. Cassirer believes it is possible to determine this point by examination of the spinal fluid.

The author takes up the question of therapy, especially from the operative standpoint. It is advisable to remove as few arches as possible, but one should not hesitate to remove as many as are needed. A kyphosis rarely develops, and other serious complications are unknown. Removal of the tumor is usually comparatively simple. If situated on the anterior side it may be missed, and it requires considerable care in manipulation to obtain a good view of this portion of the cord. Intramedullary tumors are more difficult to remove, and the result is not always gratifying. To determine the level of the tumor at the time of operation the Queckenstedt sign is of value. If the dura is punctured and there is a free flow of fluid with pulsation, the tumor may be assumed to be located caudally. If the flow of fluid is diminished, of

yellow color, and no pulsation, the tumor in all probability will be above the site of exploration. It may also be possible that the process is due to some cord change. In such a case the exploration does no harm and may even do good. In so-called pseudotumors of the cord it is usual, at postmortem, to find some cord change or the tumor situation at a different level. Following operation, symptoms may be aggravated for a while. In the course of a few days improvement in sensation occurs and later in motility. The author and others have seen complete recovery occurring in from four to six weeks. It may, however, require a year.

The regression of symptoms may pass through the same stages as the development. Ataxia may develop as a result of pressure on the posterior columns. Mild spasms, increased reflexes, plantar, extension, may remain as residuals. Bladder symptoms disappear early as a rule. The opposite is usually true in caudal tumors. According to Oppenheim and others, from 50 to 65 per cent. of the patients are cured by operation. In the past few years the author has had twenty-one cases. Of eight patients with dural tumors, five recovered completely; of seven with caudal tumors, three recovered completely, two were much improved, one with a tuberculoma, was somewhat improved; one did not improve and died. Two patients with multiple sarcomatosis of the pia were unimproved and died shortly following operation. The four remaining patients, one with a huge intramedullary glioma, died soon after operation; in one cystic changes of the cord were found with slight improvement after operation. In the two others the subsequent history is not known.

MOERSCH, Rochester, Minn.

ON STRUCTURAL LAWS IN THE NERVOUS SYSTEM; THE PRINCIPLES OF NEUROBIOTAXIS. C. U. A. KAPPERS, Brain **44**:2 (July) 1921.

The author first states the points of view of various embryologists on the subject. Hensen said "all nerves originated by an insufficient separation in the primary connections between ganglion cells and their peripheral organs during evolution." Sedgwick is quoted as remarking that "nerves are developments of the reticulum, elongated strands of pale substance composing this reticulum with some of their nuclei." Balfour and His believed that the connections of the nerves with their end organs were secondarily acquired. His saw in it a particularly mechanical problem of embryonic evolution wherein the direction assumed was determined by paths of least resistance. Dustin saw preformed forepaths enabling him to interpret regenerative phenomena in the peripheral nerves. He contrasts the failure of regeneration in the central nervous system and attributes it to an absence of the sheath of Schwann.

Kappers, seeking a clear explanation, fails to find the answer in the conception of the embryologists. He mentions Cajal as being the first to pronounce a tropistic influence, and develops a theory along similar lines. Cajal believed that the connections of the nervous elements are determined by the secretion of "attracting and repulsing substances" and by the sensibility to these substances in the ganglion cells. The chemotactic substances, he states, may be secreted by ependyma cells and also by different parts of the central nervous system, and may enter this stage of secretion at different periods of embryonic development. Conspicuously lacking is any explanatory statement concerning the factors which determine the evolution of the cells and the subsequent secretion

of chemotactic substances. Kappers, who had arrived at a similar interpretation of the shifting of cells in embryonic development through studies in comparative phylogenesis, carries the problem a step farther in trying to explain the factors which determine not only the evolution of the cell per se and the subsequent secretion of chemotactic substances, but also the formation of nerve fibers, especially in the central nervous system, and the delicate functional relationships which result.

He believes that the shifting process is very common, and that it is determined by a process of taxis or tropism caused by the stimulation of such cells and their "bio-electric consequences" which determine also the selectivity in neuronal connections and the difference between dendrites and axons, the so-called "dynamic polarization of the neuron." This was elucidated by a study of the topographic differences of homologous cell groups in vertebrates, particularly the motor roots of the oblongata, cord and midbrain. It was found that such topography was determined by the places from which the largest number of excitations reach the cells, that is, with the increase of stimulations in a certain tract, certain cells of the bulb approach this tract and do not migrate to tracts that are not related to it in function. For instance, axonic connections between the visual and vestibular impressions often reach the brain simultaneously.

The author formulates the following: "1. If several stimulative changes occur in the nervous system the outgrowing of the chief dendrites and eventually the shifting of cells takes place in that direction whence the largest number of stimulations goes to the cell. 2. This outgrowing or shifting, however, only takes place between stimulatively correlated centers; temporarily correlated excitation acts a part also in the connections of the axons."

Taking up the dynamic polarization of the neurons, he states that there is a stimulopetal tropism with the dendrites, whereas in the axons there is an irradiation of currents from the center—a stimulofugal process. He quotes Bok who found that when a bundle of unmedullated nerve fibers grows out, passing neuroblasts on its way, the neuroblasts become activated by that bundle and send forth an axon in a direction perpendicular to the activating bundle. This fact was established by finding that neuroblasts lying at a distance from the activating bundle apparently were not activated. The functional end connections of the neuron is attributed by the same writer to a stimulative relationship between the place where the axon starts and the region in which it will end.

Kappers believes that neuroblasts and "placode cells," so long as they have not developed dendrites, may shift with the nervous currents away from the excitation center, but that ripe ganglion cells will not do so. This led to the inquiry as to the determination of the stimulopetal tropism of the dendrites and the stimulofugal tropism of the axons in one and the same cell. It is concluded that a bio-electric influence, galvanotropism, is the leading factor. This is explained as the phenomenon seen in living beings whereby that being or a part of it has the inclination to turn to a certain pole—usually the negative—when influenced by a constant electric current of a very low potential. The reverse process may also be true if the solution of potassium salts is stronger. Cataphoresis in albumin-like materials is compared to nerve constituents and conclusions are reached to the effect that there is a connection between the physiology of excitation and conductivity and a reversible process. A part of the surface of a nervous leader, in excitation forms a cathode with regard to its surroundings—an anodic field. The nerve cells in the proximity of the

electro-negative excitation center first produce a positive offshoot corresponding to the irradiation of the nervous current from the excitation center, which is the katonic axon. The positive ions play an important rôle, then, in axon growth, comparable to the part played by different concentrations of electrolytes in the nervous current itself. The axon contains large quantities of potassium compounds, which must favor the stimulo-concurrent character of nerve fibrillae lying in it. Ingvar confirmed the foregoing hypothesis by finding that the outgrowth of the axon may be determined by a constant galvanic current of certain strength. At a much later stage the dendrites appear coincident with the formation of Nissl-bodies which contain oxydases and catalases. At a still later time the cell body shifts toward the center of excitation—in an opposite direction to the axon. The dendrites then have a galvano-tropism directly opposite to the galvano-tropism of the axon, the whole being in perfect harmony with the phenomena of excitation and contraction at the cathode, according to Pflüger's law.

The cathodic shifting of the dendrites and ripe ganglion cells occurs only with those parts of the neuron which contain Nissl substance, whereas the axon, which contains no Nissl-substance, shifts in the opposite direction. The Nissl-substance at first is in a fluid state surrounding the fibrillar structure and contains oxydases—an acid derivative, for example, a compound of nuclein acids and iron. "The liberation and accumulation of the Nissl-substance at the pole of the neuron that is opposite to the potassium accumulation agrees with electrolysis."

Monaxonism and polydendritism are similarly explained. The former necessitates the realization that with a polar tropism the object under influence of a bio-electric current places itself so that the influence is equally great on both sides of the object, producing an equilibrium. When two or more excitation centers simultaneously activate one cell the axis cylinder grows out in the resultant line of both current directions, since it is only in this line that an equal influence of the activating centers is exercised. When one comes after the other, however, the first causes the formation of the axon hillock, and those currents coming afterward utilize the greater conductivity of this zone. This point becomes the favorite conveying path for all stimuli running over or through the cell body. Polydendritism depends on the reaction of the protoplasm which shifts in the direction of stimuli appearing in the vicinity of the cell. Monoaxonism, then, is the result of polar localization of the anodotropic part of the cell, whereas polydendritism is based on the fact that the cell plasm has no place of predilection and is everywhere sensitive to the cathodic tropism.

The selectivity in the formation of neuronal connections is based on the synchronic or immediate successive function of the elements. The budding cone of the axon is the positive potential and cells, which are near it in a state of ionization, present a selective point to the budding axon. Thus the cell or dendrites with which it is going to be connected (synapse) are those which have been stimulated by an action current and present a predilection point. A cell with an immediately preceding state of function forms a center of attraction for budding axons, and the same is true for the muscle contractions which attract the nerve fiber to it in growth. The broad general idea evolved is that during the evolution of tissue, electric conditions occur which are very similar to those which take place in stimulation, and thus connections are made between the nerve fibers and the parts they activate.

PATTEN, Philadelphia.

DIAGNOSIS AND TREATMENT OF MENINGITIS OCCURRING IN AURAL CASES. Charles Ballance, Brit. M. J. **2**:399 (Sept. 10) 1921.

This well-known surgeon states that meningitis is the most complex and dangerous complication of aural disease. He believes that the persistence of disease of the temporal bone is the indication for operation and that one should never wait for the onset of an intracranial complication. In discussing illustrative cases, this author repeatedly points out that the operation in acute mastoid inflammation is not complete until lumbar puncture has been performed. In posterior basic meningitis, Ballance advocates draining of the cisterna magna and breaking through the pial expansion forming the posterior half of the roof of the fourth ventricle.

A CASE OF MYOPATHIC MUSCULAR ATROPHY IN A NEGRO. J. F. Corson, J. Trop. M. **24**:234 (Sept. 1) 1921.

Corson reports a case of Erb's juvenile type of myopathic atrophy in an 18 year old negro boy, with atrophy and weakness on voluntary movement of the trapezius, latissimus dorsi, pectoralis major, biceps cubiti, brachialis anticus, triceps extensor cubiti, supinator longus. Voluntary movements of the serratus magnus were lost. Pronation and supination could be performed. The mobility of the scapulae was increased. The thigh muscles were wasted and weak. The gait was waddling. The erect posture was assumed by the characteristic method. Muscles of the face were not involved. Aphonia was present.

THE SUGAR CONTENT OF THE CEREBROSPINAL FLUID AND ITS DIAGNOSTIC VALUE, ESPECIALLY IN LETHARGIC ENCEPHALITIS. R. Coope, Quart. J. Med. **15**:1 (Oct.) 1921.

The author, summarizing the findings of numerous writers on this subject, calls attention to two points: 1. A high sugar content should not be regarded as a positive diagnostic sign of lethargic encephalitis. 2. A low sugar content (provided the fluid is fresh) is a strong indication of an acute or tuberculous meningitis. Coope examined the cerebrospinal fluid of ninety-five patients for its sugar content, using the method of Folin and Wu for blood sugar. His three normal fluids gave 64, 69 and 83 mg. per 100 c.c.; the eleven cases of lethargic encephalitis varied from 67 to 94 mg. per 100 c.c.; twelve cases of tuberculous meningitis from 18 to 55 mg. per 100 c.c.; one case of pneumococcic meningitis, 19 mg., and one of meningococcus meningitis 8 mg. per 100 c.c.; four cases of syphilitic meningitis 72-100 mg. per 100 c.c. He concludes that the French tendency to regard a high sugar content of the cerebrospinal fluid as diagnostic of lethargic encephalitis is not justified, but that a low sugar content, especially one below 40 mg. per 100 c.c., is strongly in favor of an infective meningitis.

A CASE OF JUVENILE GENERAL PARESIS. G. J. Key and A. Pijper, South African Med. Rec. **19**:343 (Sept. 24) 1921.

The father gave a four plus complement-fixation test for syphilis, and the third child (aged 6 years), in a family of five, a plus-minus reaction. All members of the family except the patient were in good health, and there was no history of miscarriages or stillbirths. When the patient was 6 weeks old

he had several convulsions. At 10 months of age he suffered with "sores all over the body." He attended school from the fifth to the seventh year and progressed rapidly. During his eighth year he had to be returned to a lower grade, and then became indolent, irritable and lost interest in his books. In his ninth year he slept poorly and was often noisy at night. When about 10 years old his parents realized that he was failing mentally. He became careless in his habits and personal appearance and had some difficulty in walking. From the tenth to the twelfth year he failed rapidly; he lost all interest in his surroundings, his speech became defective, he would scream without apparent cause, he became slovenly in his habits and had to be fed. His gait was so ataxic that he fell when he attempted to walk. He could utter only a few words but gave signs that he could recognize his parents. On admission to the Mental Hospital he showed no signs of congenital syphilis. However, his pupils were dilated, irregular and did not react to light. The tendon reflexes were exaggerated but equal; ataxia was marked; there were fine tremors of the lips and tongue and his facial expression was vacant and silly. The Wassermann serum reaction was four plus. One month after admission he was unable to articulate but mumbled unintelligibly. The lower extremities were useless, the feet were dull blue. During the fifth week gangrene of both feet was present; on the left the line of demarcation was over the distal ends of the metatarsals; on the right the gangrene extended to the middle of the metatarsals. There was incontinence of urine and feces. Six weeks after admission, the hands, upper lip and tip of the nose became blue, and the skin peeled off when an attempt was made to wash them. Later he had difficulty in swallowing and was unable to retain even milk. Death occurred seven weeks after admission to the hospital.

The report of the necropsy covers the brain only. These authors report the usual external and internal hydrocephalus, but no granular ependymitis of the ventricles, and marked thickening of the pia-arachnoid, especially over the frontal and parietal regions. Microscopically the cortical cell devastation was marked in the frontal lobes, less so in the parietal and temporal portions, and almost negligible in the occipital lobes. The glia cell proliferation was most marked in the parts showing greatest nerve cell destruction. Vascular changes were prevalent in all parts of the cortex and varied from slight perivascular infiltration with plasma cells to complete destruction of the vessel, with hyaline degeneration. In some areas almost normal vessels appeared in close proximity to those showing marked infiltration and hyaline degeneration. Stäbchenzellen were found in many sections. In the cerebellum the cell devastation and vascular changes were less marked. Double nucleated Purkinje cells were observed only once or twice.

In view of the marked vascular changes reported in the brain and the clinical evidence of disease of the vessels of the extremities and face, it is to be regretted that the pathologic condition of the whole arterial system was not studied.

TUMOR OF THE SPINAL CORD. J. M. Gill, M. J. Australia **2**:201 (Sept. 10) 1921.

This author cites the case of a woman, aged 68 years, whose history was uneventful until eleven months prior to her admission to the hospital, when she complained of severe attacks of pain radiating from the spine at the level of the sixth rib, which became so severe that her legs grew weak and stiff.

Fourteen days before admission there was some loss of control of the bladder and of the rectal sphincters, and painful involuntary movements of the lower extremities. Examination revealed: (1) a paralysis of both lower extremities, with the hips and knees semiflexed; (2) involuntary drawing up of the thighs with flexion of the knees; (3) pain in the back between the angle of the left scapula and spine and under the left breast; (4) some loss of control of the bladder and rectal sphincters; (5) a sense of constriction about the waist. The superficial abdominal reflexes were absent; the knee reflexes were slightly increased; the Babinski sign was positive on both sides; ankle clonus was absent. There was tenderness to pressure over the fourth, fifth and sixth dorsal spines, and sensory tests were unsatisfactory on account of the pain produced. At a later examination there was complete anesthesia for pain below the kness, with impaired sensation from the knees to the level of the tip of the sternum. Still later the loss of pain sense was complete up to the level of the xiphisternal line and an hyperesthetic zone about the level of the eighth dorsal spine. Gill made a diagnosis of meningeal tumor of the spinal cord at the level of the sixth dorsal root. At operation a tumor measuring 5 cm. in length was found loosely attached to the arachnoid at the level of the fourth dorsal vertebra. The spinal cord was flattened and did not pulsate. Microscopic examination showed that it was an endothelioma. On discharge from the hospital three months later, the patient could move her legs slightly, sensation was present up to the knees, and the control of the bladder was improved. The author remarks the rarity of such a case in a person aged 68 years.

THE PHYSIOLOGY OF SYMPTOM PRODUCTION IN DISEASE AND INJURY OF THE NERVOUS SYSTEM. F. M. R. Walshe, Brit. M. J. **2**:377 (Nov. 19) 1921.

Jackson's theory of the dissolution of function of the nervous system, the phylogenetic hypothesis of Head and Rivers and the psychic origin of disorders of the body function are discussed briefly and condemned by Walshe. The author then turns to the physiologic factors in the production of symptoms in disease and describes in detail the effect of anoxemia (oxygen-want) in the activity of the nervous system. Acute anoxemia results in defect of memory, attention and judgment associated with marked emotional disturbances, muscular spasms and twitchings, weakness, tremor and ataxia with parasthesias and sensory impairment. Visual and auditory acuity are diminished. These symptoms are transient, and if the anoxemia is of short duration do not result in permanent defects of function. The effects of oxygen-want are seen in the convulsions of the asphyxial states and in the epileptiform seizures which often usher in a cortical thrombosis or accompany free hemorrhage from any part of the body. Irritative symptoms indicative of beginning compression in traumatic intracranial hemorrhage are associated with cyanosis, that is, deficient oxygenation of the brain. When compression renders the affected area of the brain anemic, irritative symptoms give place to paralytic.

Jacksonian seizures in patients suffering with depressed fractures over the motor cortex depend on compression of the cortex and interference with its circulation and not on the irritation of these areas by indriven bone. Walshe believes that the discharges from an hyperexcitable center are not only exaggerated but that they are also altered qualitatively. He doubts that irritative symptoms ever occur apart from impairment of functional efficiency.

## BILATERAL RIGIDITY IN MIDDLE MENINGEAL HEMORRHAGE.

GEOFFREY JEFFERSON, Brit. M. J. **2**:432 (Oct. 21) 1921.

After calling attention to the fact that the literature of middle meningeal hemorrhage shows only a few cases with general muscular rigidity, Jefferson reports two cases which may be summarized as follows: Both were in men aged 37 and 26, respectively. One fell from a first story window, the other 60 feet from a roof. Neither were unconscious until about one hour after their accident. When seen by the author seven and three hours after their admission to the hospital the patients presented bilateral rigidity. The lower extremities were extended and strongly adducted. The feet were plantar flexed and inverted. In the first case the rigidity was so marked that considerable force was necessary to change the position of the limbs and any attempt to move them increased the rigidity and produced a fine tremor. In the second case there were tonic contractions of the limbs every three or four minutes, with a marked increase in the rigidity. In his first case the arms were held rigidly extended at the sides with the forearms hyperpronated. In his other case the left arm was extended stiffly in slight abduction, the wrist flexed and adducted; the fingers were partly closed and the thumb adducted. The right arm was flexed (130 degrees) at the elbow, fully flexed at the wrist and the fist held as on the left side. During the seizures the upper extremities presented the same picture as in Case 1. Both patients developed Cheyne-Stokes breathing, and their muscular rigidity was markedly increased at the height of the respiratory movements. In Case 1 the head was turned sharply to the left as were the eyes. The patient in Case 2 showed no rotation of the head. Opisthotonos was present during a few of the tonic seizures in Case 2. The patient in Case 1 presented a widely dilated left pupil. Tendon reflexes were elicited during the interval between seizures in Case 2 but were not demonstrable in Case 1. Ankle clonus was present in both cases, also Babinski's reflex. The abdominal reflexes were absent on the left and reduced on the right side in Case 1. Both patients were operated on by the author. The patient in Case 1 presented a fracture in the anterior part of the left temporal fossa and an extradural clot 12 cm. in diameter and nearly 4 cm. in depth at its thickest part. The clot lay over the left frontal lobe and extended forward and upward. The dura was not opened. The rigidity disappeared at the completion of the operation. Death occurred three hours later. At necropsy nothing further of interest was found. In Case 2, under local anesthesia, a depressed fragment of the right frontal bone 8 by 4 cm. extending up to the midline was elevated and removed. A small clot was found overlying the anterior end of the superior longitudinal sinus. The right orbital plate was comminuted and the dura torn. The patient became flaccid, the seizures ceased and the pulse fell to normal. Two hours later the pulse increased, and he died seven hours after operation without any return of the rigidity. At necropsy an extension of the fracture was found over the left frontal bone with a laceration of the left middle meningeal artery. The resulting hemorrhage was the size of a man's fist and lay over the frontal pole of the left hemisphere.

In conclusion the author states that the rigidities in his cases must have been dependent on changes in the intracranial circulation produced by the extravasations of injury and could not be the result of local irritation. The clinical syndrome depends on a relative deficiency or the reverse of the blood supply to certain regions of the brain and results in the release of lower

neuronic levels. It is probable that this syndrome in man depends on a fine circulatory balance, on a relative anoxemia sufficient to suppress cortical control but not great enough to render inactive the causal mechanism in the midbrain and hindbrain.

CRIME AND MENTAL DEFICIENCY. W. C. Sullivan, Lancet **201**:787 (Oct. 15) 1921.

Sullivan in his lectures on mental deficiency at the University of London states that conduct may be criminal, but there are no criminal aptitudes, and it is only rarely and in a more or less figurative sense that we speak of criminal impulses. Most crime that is not professional is due to the failure of inhibitory control, or an inability to refrain from the immediate satisfaction of impulse. This failure may be the result of an unduly strong impulse or a weakness of the power that should control and direct it. A study of statistics shows that the proportion of criminals to the population of the same age is at its highest during the period of adolescence, that is, between the ages of 16 and 21 years. The author believes that this is what we should expect if crime is due in any important measure to weakness of inhibitory control. While the impulses of the feeble-minded do not exhibit any constant difference from those of normal persons, it is not uncommon to observe instances in which mental deficiency is associated with an excess or perversion of instinctive activities leading to criminal acts which seem to be related more to abnormality of impulse than to failure of inhibition. Inadequate capacity of control is a regular or permanent feature in many cases of mental deficiency and is presumably the source of the special criminal proclivity characteristic of the mental defective whose mentality is that of an adolescent. The mentally defective person may and often does commit crimes because his mentality does not permit the realization of the consequences of the act. The moral imbecile is not simply an amoral person, he is an amoral person whose debility is more prominent in the sphere of the emotions and the will, but who presents some degree of intellectual deficiency. The author calls attention to the frequent occurrence of moral imbecility in the offspring of epileptic stock, to the occasional supervention of epileptic seizures in the later life of this group, and to the fact that a condition resembling moral imbecility may be the result of a retarded development and not to a permanent deficiency. The pathologic swindler whose ethical defect is of a less generalized character should also be classed as a moral imbecile.

ENCEPHALITIS LETHARGICA. Edwin Bramwell, Brit. M. J. **2**:648 (Oct. 22) 1921.

At the annual meeting of the British Medical Association, Bramwell summarized the investigations of many authors on epidemic encephalitis. He called attention to the signs and symptoms, which he considers of particular diagnostic importance: (*a*) ophthalmoplegia of central origin of more or less acute onset, which sooner or later shows a tendency to improve; (*b*) transient diplopia at the onset of the illness; (*c*) nystagmus, which may vary in rapidity, amplitude and direction; (*d*) paralysis of conjugate upward movement of the eyes associated with little or no impairment of ocular movement; (*e*) drowsiness and lethargy of varying degree accompanied by intelligent though slow response to questions; (f) the masklike face and postural attitudes, suggestive of paralysis

agitans; (g) mental disorientation similar to that seen in chronic alcoholism, and (*h*) myoclonic, athetoid and choreic movements.

POTTER, Mercer, Pa.

PROGRESSIVE LIPODYSTROPHY. W. M. KRAUS, Rev. neurol. **28**:357 (April) 1921.

Kraus presents a clear-cut case, the twenty-third of the typical form to be reported. The patient was a young woman, aged 22, with an apparently otherwise negative personal and family history, in whom the lipodystrophic state had existed for fourteen years. At the time of examination the cardinal features of the disorder were typically present—relative and symmetrical wasting and reduction of adipose above the level of the first lumbar segment, particularly of the face and thorax, with marked fatty increase, also symmetrical, below this point, especially of the thighs and buttocks. The legs, to the ankles, were abnormal in size, giving the impression of a hard edema but without pitting—in fact, strikingly of the trophedematous cast—and the skin was observed to be rather thick and rugose.

The author comments on the obscurity of the actual etiology and pathology in this condition, directing especial attention to the occurrence of certain fundamentally resemblant features in both this disturbance and trophedema. He suggests that progressive lipodystrophy might conceivably be regarded as a basically trophedematous state with superadded fatty changes in the subcutaneous field, thus emphasizing from a somewhat different angle, the possibility mentioned by Boissonnas, of underlying autonomic imbalance or dissociation as of fundamental significance in the etiology of this disorder.

There are two excellent illustrations.

CRANIAL DYSTROPHY SUGGESTING OXYCEPHALY. E. D. PAULIAN, Rev. neurol. **28**:358 (April) 1921.

Paulian's case was that of a woman, aged 30, presenting a rather striking anomaly of skull contour associated with loss of vision and rather frequent epileptiform attacks. According to the history, the patient had suffered an attack of "cerebral fever" at 18 months, followed by typhoid three years later. At 5 she suddenly became blind; about this time, a rotary nystagmus and exophthalmos also became manifest, the latter, seemingly, having become progressively more marked. Epileptiform attacks, rather typical in type, first appeared at 15 and had been noted ever since, occurring at intervals of four or five weeks, both nocturnally and during the day. Headache was not reported, and no mention was made as to psychiatric or endocrino-autonomic status.

Examination revealed definite, although not extreme, flattening of the skull transversely, especially anteriorly, with slight prominence of the superior frontal border, great diminution as to the frontal bosces and leveling of the superciliary ridges, with some degree of depression of the bones of the face and obliqueness of orbital alinement. Roentgenologic study of the skull revealed marked basal lordosis with effacement of the orbital and sphenoidal sinuses, enlargement of the sella which appeared to be of the bilobic type and slight bregmatic prominence, with no indication, however, of intracranial ridging or digitation. In that sense, and in view of the flattening of the vertex and the absence of turricephaly, the picture was somewhat atypical as regards the classical oxycephalic type. There was, in addition, marked

exophthalmos and rotatory nystagmus, bilaterally, with distinct outward and downward direction of the eyes. The pupils were dilated, with fixation to light, and ophthalmoscopic examination revealed marked bilateral optic atrophy of the postinflammatory type. The right leg was 8 cm. shorter than the left and definitely atrophic in all dimensions.

In view of the early history and but partial oxycephalic syndrome, the author is disposed to regard this case as basically representative of postencephalic sequellae of long standing in a person presenting the oxycephalic skull type in intermediate degree and probably not of itself sufficient to account for the clinical symptomatology as determined.

OCCUPATIONAL DYSKINESIA—PARESTHETIC TYPE. C. HOULLION, Rev. neurol. **28**:348 (April) 1921.

The author comments on the perplexing problem presented by the occupational spasms, so-called, directing attention to the importance, in this field, of Duchenne's work, according to which such disorders are classified as motor and sensory, including under the former the akinetic, hyperkinetic (classical cramp) and ataxic (tremors, choreiform and ataxic movements) types. The purely sensory type, of which Houllion's case is an example, is deemed extremely rare, but, on the other hand, sensory disorders of some kind, such as anesthesia, paresthesia and "neuralgia," are frequently encountered as complicating features in the more essentially motor types.

Houllion's case was that of a seamstress, 56 years of age, with a negative family and personal history, except that both the patient and her mother were described as of a "nervous" temperament. The present trouble dated back three years and manifested itself primarily as a severe tingling and numbness in the fingers and hand (right), occurring characteristically in the morning, particularly after the patient had sewed for a long time or had done extensive laundering the preceding day. This trouble was usually first noted about fifteen minutes after she commenced to sew in the morning, and beginning in the finger tips, gradually extended so as to include the entire hand, with short periods of intermission, continuing until it was no longer possible to hold the needle. At such times the hand appeared ischemic with an accompanying sensation of frigidity but with no associated spasm or rigidity. On dropping the needle and holding the hand pendent or immersing it in hot or cold water, the paresthesia soon disappeared, only to recur, however, on the resumption of sewing. This situation would repeat itself from six to eight times, following which the patient was able to sew for the balance of the day without further discomfort. Curiously, no disturbance was found to occur if the patient preceded her morning sewing by a period of other work, and no difficulty was ever reported at night. The course of the disorder had apparently not been progressive and had been marked by phases of complete remission over periods—one of them several months in duration—when needlework had been discontinued.

Neurologic examination was negative except for slightly increased sensitivity of the right arm trunks to electrical stimulation.

Mention is made categorically of the various hypotheses which have been advanced as to etiology, the author seeming to favor that of perverted vasomotor habit or "neurosis" dependent, presumably, on basic autonomic imbalance or dysfunction.

PATHOGENESIS OF GENERAL PARESIS AND TABES. A. SEZARY, Rev. neurol. **28**:337 (April) 1921.

Sezary directs attention to the rather striking contrast between general paresis and tabes and syphilis of the more essentially somatic or constitutional type, particularly as to the late cutaneous and visceral forms with which the former are often associated. These constitutional lesions for the most part are essentially sclerogummatous in character, while the neurosyphilitic changes, particularly those of paresis, are primarily not of this type, representing rather a perivascular and interstitial inflammatory reaction with specific associated cell and fiber alteration. The sclerosis that occurs is construed as secondary to preceding neuraxial degenerative change; as a matter of fact, according to Sezary, the general histopathology here is, in a measure, rather suggestive of the chancre type. It is of peculiar significance also that in these disorders, especially the paretic type, spirochetes are practically never found in the meninges although they are abundantly determinable in and about the cortical cells. Of interest, too, is the fact that the spinal fluid in these cases is usually avirulent and that the blood Wassermann reaction is generally reducible while that of the fluid is not. The author therefore feels that such disorders are due to primary spirochetal change in the neuraxial tissue associated with transient or intermittent humoral invasion. From this standpoint, Sezary concludes that neuraxial tissue possesses a certain partial natural immunity against the spirochete, of sufficient degree in most cases to inhibit greatly or to retard the development of these organisms, which probably reach the neuraxial field rather early in the infection, and as a result of which these tissue elements do not participate in the general constitutional immunization effected shortly following secondary systemic spirochetal invasion. Finally, however, in many cases the latent neuraxial infection is able to break through this local inhibitive influence and develops lesions of a primary diffusely inflammatory and degenerative type, quite atypical, as indicated, in comparison to those characteristic at this time of the constitutional or more essentially humoral field.

There is a relatively meager therapeutic response in neurosyphilis, particularly as regards the arsenicals, because, according to the author, this type of tissue, owing to its peculiar chemism, appears unable to oxidize properly such compounds, a step, seemingly, absolutely sine qua non to the effective mediation of specific pharmaceutical reaction.

RAPHAEL, Ann Arbor, Mich.

STRATIFICATION IN HYPNOTIC SELF-OBSERVATION. J. H. SCHULTZ, Monatschr. f. Psychiat. u. Neurol. **49**:137 (March) 1921.

The author reports the results of his experimental observations.

The tests are carried on with the patient lying in a darkened or half darkened room. The eyes are kept closed, and he is told to note the subjective phenomena occurring in the "visual field" and to describe exactly what he sees.

The material always appears in three forms, which follow each other as the hypnosis gradually deepens.

1. The first layer consists of the usual formless colors, spots, veils, lines, half shadows, lattice, rings, etc. They are localized "in the eye" or "in the field of vision" and are often spontaneously compared with after-images. This stage of "raw material" is often very short, and may be overlooked unless attention is directed toward it.

2. The second stage is the stage of thought visualization. Usually it appears as the finished thought product—as a picture localized in the visual field. Occasionally the picture is seen forming from individual elements, and when formed, passes out like a moving picture film, the patient feeling himself the observer.

3. The third stage is quite different. Things appear which have a definite sense of reality but which are entirely foreign to the person—often things of fantastic form and size, with curious color schemes and without comprehensible meaning. Undoubtedly in this third layer lies much of the material which in pathologic cases contributes to the material of hallucinations.

In the first two strata, composed respectively of formless visual material and visualized thought, the material is appreciated as belonging to the individual. The third layer, primitive layer, contains material foreign to the individual (unconscious). It is remarkable that the third layer can be reached without the developing of amnesia on awakening. Certainly it represents a physiologically changed state of the brain. It is probable that the majority of normal night dreams run their course in the second layer, especially the connected, episodic dreams of light sleep. When dreams reach the third layer, they are probably difficult to recall, just as this same stage is difficult to recall in hypnotic self-observation.

BRAIN TUMORS (NOTES ON THE QUESTION OF CEREBRAL LOCALIZATION). HERMANN FORTIG, Monatschr. f. Psychiat. u. Neurol. **49**:89 (Feb.) 1921.

When one considers how intimately the various portions of the brain are connected with each other, and how profoundly one part is affected by damage to a distant part (Monakow's diaschisis), it becomes impossible to believe in any strict theory of localization which places in a circumscribed area of the brain a definite group of concepts or sector of intelligence. On the other hand, there is no question but that different cerebral zones are functionally different. The mass of facts already accumulated bearing on the problems of cerebral localization is so great as to be confusing.

Rieger has attempted to view the whole problem from a simplified point of view. He divides the brain into two portions, forebrain and hindbrain, the line of division being the central sulcus. To the hindbrain he attributes the general function of perception; to the forebrain, ideation. Fortig calls attention to the fact that this division corresponds with Kant's division of the sources of all human knowledge into two—perception and ideation.

In line with Rieger's view is the fact that anatomically we find all the sense organs represented posterior to the central sulcus. These sense centers, however, occupy only a small part of the hindbrain. A much larger part is taken up by the extensive temporo-parieto-occipital association tracts. This great association zone was formerly looked on as a silent area, but now is known to be directly concerned with the formation of spatial concepts. Fortig discusses in some detail the ideas of the Würzburg school (to which he belongs) relative to spatial concepts. All objects that we see and feel are seen and felt as "circumscribed space." The various disturbances in our knowledge of the outside world which have been grouped under the various titles of mind-blindness, astereognosis, agnosia and asymbolia, are essentially dependent on a disturbance of the spatial concept. The patient who is mind-blind sees, but the object at which he looks is no longer recognized in its spatial relations. The same is true of many apraxias, agraphias and alexias.

In the hindbrain are located perception and spatial orientation; in the intermediate zone, between the forebrain and hindbrain, motor and sensory speech; and in the forebrain, ideation. The author conceives as the characteristic function of the forebrain the grouping of lower concepts to higher and higher abstract units—ideas. He grants that this conclusion is based on exclusion and not on anatomic foundation. Certain facts seem opposed to it, especially those cases of frontal lobe lesions with "negative" findings clinically. But, as the author points out, we are totally incapable of appreciating the finer changes in the psychic life of a person. People vary so in their capacities and their acquirements that what is normal for one is subnormal for another, and only grosser changes are manifest. As an additional function of the forebrain, first described by Auerbach, he mentions lack of initiative.

Summary: The hindbrain serves chiefly perception and spatial orientation. The forebrain serves the higher abstract world, the world of initiative. In between lies the central brain which is the world of conscious acts, including motor speech. But this is not a strict localization, for he recognizes that functions assigned to the various parts are merely predominantly in these parts. We must consider the whole brain as an intricate network with here and there zones of specially increased density to serve special functions. The essence of our psychic life is a binding and grouping of the most complex order, and if we will interpret it we must approach the problem from the dynamic standpoint.

# Society Transactions

## BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

*Regular Meeting, Jan. 19, 1922*

JAMES B. AYER, M.D., *President*

### PRELIMINARY REPORT ON EXPERIMENTAL CONVULSIONS: CONVULSIONS PRODUCED BY ADMINISTRATION OF CHEMICAL SUBSTANCES.

Presented by DRS. SCHICHI UYEMATSU and STANLEY COBB.

Epileptiform convulsions can be produced by the administration of various chemical substances. So far as we are able to ascertain from the literature, enchonidin, picrotoxin, and absinth appear to produce convulsions very similar to those of epilepsy.

Following an injection of wormwood oil in a dose just sufficient to produce convulsions (0.04-0.07 c.c.), a rabbit, after from three to ten minutes, becomes quiet and then begins to tremble; light twitches of the face, ears and neck muscles follow, becoming stronger and stronger; then a clonic convulsion of rapid tempo (tonic) occurs immediately, first in the forelegs, afterward in the hindlegs. The head is drawn backward on the neck, the forelegs stretching forward in tonic spasm. With the violent convulsions the animal moves involuntarily backward. During these generalized convulsions clonic champing of the jaws, marked frothing at the mouth, crying and involuntary urination and defecation are noticed. In this period the pupils are dilated. The clonic spasm of rapid tempo imperceptibly changes to a running motion (alternating flexor and extensor spasms) which becomes slower and slower and finally ceases. The animal then keeps quiet and appears sick, with rapid respiration and palpitation. The convulsions differ considerably, according to the dose used. The dose sufficient to cause twitching of the aural and facial muscles and slight clonic spasms of the forelegs is called a threshold dose in our experiments.

The opinions of authors differ considerably in regard to the site of discharge and the form of convulsions originating from different levels. But these differences in results of the various workers seem to us explainable on the ground of ignorance of the doses given: that is, the convulsant drug was never quantitatively controlled. Also other factors, such as anesthesia, technic of operation, ligation of vessels, etc., which would change the excitability of various centers, were not sufficiently considered.

From our own experiments (five) and a review of the literature, it seems justifiable to conclude that:

1. Convulsions can be discharged from any part of the neural axis.

2. With the cerebral cortex intact, animals show convulsions after the administration of a much smaller dose of convulsant drug than after decortication or decerebration. Spinal preparations require much larger doses to cause convulsions.

3. With the central nervous system intact or with injury to parts of the cortex not directly associated with motor activity (for example, occipital

lobes), wormwood oil convulsions are epileptiform, as described in the foregoing. After decortication, decerebration and spinal cord transection, the clonic convulsive movements are of slower tempo. In the latter case they are rapid above and slow below the cord lesion.

Having heard of the beneficial effects of fasting on patients with epilepsy treated by Dr. H. M. Conklin of Battle Creek, and having observed the work of Dr. H. R. Geyelin of the Presbyterian Hospital in New York, we undertook experiments to find out whether fasting in animals would reduce their susceptibility to convulsions. The convulsions were produced with wormwood oil, and each rabbit was carefully tested out to ascertain his threshold dose. The results of starvation are shown in Table 1.

This work is open to the criticism that the doses are so small that a mistake of 20 or 30 per cent. might easily be made.

The effect of starvation seems to be to reduce the susceptibility of rabbits to convulsions. Just what factor in starvation is responsible for this effect is difficult to determine. One possibility seems to be the lowered metabolism known to accompany starvation. We therefore took a series of rabbits and intoxicated them with thyroxin. The effect in relation to convulsions is seen in Table 2.

Again there is decreased susceptibility to convulsions; this time with metabolism raised. Therefore, changes in basal metabolism would seem to be ruled out as an important factor in the production of convulsions.

A third series of rabbits was operated on for thyroid removal. The results of experimental convulsions on those that survived long enough to have a reduced metabolism is indicated in Table 3.

Thyroidectomy apparently increases the susceptibility of rabbits to convulsions. This result is in accordance with similar experiments carried out by J. and H. Fischer. They state that thyroidectomized animals are more susceptible to amyl nitrate convulsions than normal animals.

Before we can draw any conclusions as to the factors which increase or decrease the susceptibility of the animals to convulsions, obviously we shall have to test out other conditions which vary in such experiments.

DISCUSSION

Dr. Donald Gregg: In the starvation treatment, do you differentiate between fats, sugars and proteins, or do you cut them off altogether? Are liquids also curtailed? And if so, is not the decrease in convulsions possibly due to a decrease in body fluids, especially the cerebrospinal fluid?

Dr. C. Macfie Campbell: In starvation of animals there are changes comparable to acidosis.

Dr. Karl Bowman: At the Psychopathic Hospital a young girl with epilepsy was admitted who showed a basal metabolism of —21. We gave her dried thyroids, one grain a day, and the petit mal attacks which had been occurring at the rate of thirty-nine a day have not exceeded ten a day since the patient has been receiving thyroid. One day when the thyroid was omitted the attacks were much more severe. We then increased the dose to 2 grains a day, but the pulse rate is going up so that we may not be able to push it further. With one grain a day the basal metabolism was —16.

Dr. Cobb, closing: These patients were completely starved except for water which they seemed to take without difficulty. The work began following the experience of an osteopath who for ten years has been starving epileptic patients and who has reported some remarkable results. I think he says that

TABLE 1.—The Effect of Starvation on Wormwood Oil Convulsions

| Serial No. | Lab. No. | Threshold Dose | Original Weight | 3d Day Starvation | 4th Day Starvation | 5th Day Starvation | 3d Day Feeding |
|---|---|---|---|---|---|---|---|
| 1 | 70 | 0.05 c.c. Slight convulsion | 2,940 gr. | 0.05 c.c. No convulsions Wt. 2,780 gr. | 0.06 c.c. No convulsions Wt. 2,550 gr. | 0.06 c.c. No convulsions Wt. 2,300 gr. | 0.05 c.c. Marked convulsions Wt. 2,770 gr. |
| 2 | 78 | 0.04 c.c. Fairly marked convulsion | 1,770 gr. | 0.04 c.c. No convulsions Wt. 2,500 gr.? | 0.06 c.c. No convulsions Wt. 1,350 gr. | Died Wt. 1,220 gr. | |
| 3 | 90 | 0.05 c.c. Very slight convulsion | 2,850 gr. | 0.06 c.c. No convulsions Wt. 2,500 gr. | 0.06 c.c. No convulsions Wt. 2,300 gr. | 0.06 c.c. No convulsions Wt. 2,200 gr. | 0.06 c.c. Very marked convulsions Wt. 2,580 gr. |
| 4 | 91 | 0.05 c.c. Slight convulsion | 2,720 gr. | 0.05 c.c. No convulsions Wt. 2,020 gr. | 0.06 c.c. Slight convulsion Wt. 1,620 gr. | 0.06 c.c. Slight conv. Died Wt. 1,470 gr. | |
| 5 | 92 | 0.06 c.c. Slight convulsion | 2,750 gr. | 0.06 c.c. Slight convulsion Wt. 2,560 gr. | 0.06 c.c. No convulsions Wt. 2,400 gr. | 0.07 c.c. Convulsions Wt. 2,200 gr. | 0.06 c.c. No convulsions Wt. 2,510 gr. |
| 6 | 93 | 0.06 c.c. Slight convulsion | 2,860 gr. | 0.06 c.c. Slight convulsion Wt. 2,680 gr. | 0.06 c.c. No convulsions Wt. 2,490 gr. | 0.06 c.c. No convulsions Wt. 2,190 gr. | 0.06 c.c. Slight convulsion Wt. 2,590 gr. |
| 7 | 70 | 0.05 c.c. Slight convulsion | 2,770 gr. | 0.06 c.c. Slight convulsion Wt. 2,680 gr. | 0.05 c.c. No convulsions Wt. 2,380 gr. | 0.06 c.c. Slight convulsion Wt. 2,170 gr. | 0.05 c.c. Slight convulsion Wt. 2,500 gr. |

TABLE 2.—The Effect of Thyroxin on Wormwood Convulsions

| Serial No. | Laboratory No. | Threshold Dose | 1st Day, 1.5 mg. Thyroxin | 3d Day, 1.5 mg. Thyroxin | 5th Day, Wormwood Oil | 7th Day, Wormwood Oil |
|---|---|---|---|---|---|---|
| 1 | 90 | 0.05 c.c. | Pulse 135 | Pulse 204 | 0.05 c.c. No convulsions Pulse 260 | 0.07 c.c. No convulsions Pulse 250 |
| 2 | 70 | 0.05 c.c. | Pulse 136 | Pulse 170 | 0.06 c.c. No convulsions Pulse 236 | 0.07 c.c. No convulsions Pulse 220 |
| 3 | 93 | 0.06 c.c. | Pulse 140 | Pulse 180 | 0.07 c.c. No convulsions Pulse 240 | 0.09 c.c. Marked convulsions Pulse 216 |
| 4 | 122 | 0.08 c.c. | Pulse 140 | Pulse 184 | 0.08 c.c. No convulsions Pulse 216 | |
| 5 | 123 | 0.07 c.c. | Pulse 136 | Pulse 186 | 0.08 c.c. Convulsions Pulse 224 | 0.07 c.c. No convulsions Pulse 210 |
| 6 | 70 | 0.05 c.c. | Pulse 145 | Pulse 190 | 0.06 c.c. No convulsions Pulse 228 | |
| 7 | 92 | 0.06 c.c. | Pulse 150 | Pulse 180 | 0.06 c.c. No convulsions Pulse 226 | |
| 8 | 93 | 0.06 c.c. | Pulse 145 | Pulse 184 | 0.06 c.c. No convulsions Pulse 236 | |

TABLE 3.—Effect of Wormwood Oil on Thyroidectomized Rabbits

| Laboratory No. | Threshold Dose | Time After Operation | Dose | Result |
|---|---|---|---|---|
| N-21-145 | 0.05 gr. | 2½ months | 0.05 | Marked, prolonged convulsions |
| N-21-147 | 0.04 gr. | 2½ months | 0.04 | Very marked, prolonged convulsions |
| N-21-176 | 0.04 gr. | 1½ months | 0.04 | Marked convulsions |
| N-21-181 | 0.04 gr. | 1 month | 0.04 | Very marked convulsions |
| N-21-190 | 0.04 gr. | 1 month | 0.04 | Marked, prolonged convulsions |
| N-21-195 | 0.05 gr. | 1 month | 0.05 | Mild convulsions |
| N-21-199 | 0.05 gr. | 1 month | 0.05 | Marked convulsions |

he has had conspicuous improvement in about three quarters of his cases, but he has kept no satisfactory records. About two years ago Dr. Geyelin began this treatment at the Presbyterian Hospital. Some of his patients have had no convulsions for from nine months to a year and a half. This starvation effect may comprise several factors: lowering of the basal metabolism, weakness of the animal, acidosis. Answering Dr. Campbell: I think we have acidosis, but we have not followed up the biochemistry. Acidosis may be a very important factor. Answering Dr. Courtney: The blood pressure has not been studied following the thyroid feeding.

## EVALUATION OF INTELLIGENCE TESTS IN CRIMINAL CASES.

By Dr. George L. Walton.

While intelligence tests are valuable in their appropriate sphere, they are likely to prove of little aid in determining the responsibility of the criminal adult. This is illustrated by two cases. The first was that of an uneducated Italian who was self-supporting and sent money home. In company with other adults he had an altercation with an officer in the course of which he drew a revolver and shot the officer. After his arrest he denied the act and offered an alibi, but later confessed. The only material evidence offered bearing on feeblemindedness, except the Binet test, was the statement of his brother that he was not very intelligent, and testimony that he played ball, etc., during the noon hour with boys with whom some witnesses said other adults did not play; others said they did. By the Binet-Simon test his mental age was 9. To interpret the test as pointing to feeblemindedness in such a case is to underrate the most important factor in the diagnosis, namely economic efficiency, and to lay the test open to an adverse comment which it in no way deserves.

The second case was that of a young man who took part in a robbery. In making his escape he shot and killed the shopkeeper. He was examined a month and a half before the trial. At this time he correctly subtracted 33 from 100 and 15 from 50; he counted up to 20 and back with one repetition. Examined again shortly before the trial, he did so badly that he was given a mental age of 6½ by the Binet-Simon test. Examined a third time just before the close of the trial, in which feeblemindedness was a feature of the defense, he appeared unable to count up to 5, and gave other answers which taken at their face value would have indicated that he was little better than an idiot. The obvious lack of cooperation on his part, shown by the rapid apparent deterioration, counteracted whatever value the test may otherwise have had either as an aid in the diagnosis of feeblemindedness or in measuring the degree of feeblemindedness if such existed. This lack of cooperation is not unlikely to appear in the case of the criminal with a defense of feeblemindedness, whose interest is not served by the display of a high degree of intelligence.

### DISCUSSION

Dr. A. W. Stearns: I testified on the other side in this case, and I think when a person says that the Binet test is of no value he is making a rather intemperate statement, while I grant that under the circumstances outlined it is of very questionable value. The important thing in this case was the fact that the courts prior to this case had never passed on the responsibility of the feebleminded. None of the witnesses for the defense testified that this man was insane. They said that he was feebleminded and had the responsibility of a feebleminded person.

DR. D. A. THOM: When one considers this prisoner's (or patient's, as I prefer to call him) reaction and attitude to the court proceedings, his absolute lack of interest in what was going on, his inability to follow in any way the court procedure, not knowing the judge, jury, or physicians, and having little idea of who was for him and who was against him, one cannot help feeling that the man was different. When asked during the trial, "What is going to happen to you if they pronounce you guilty?" he said, "Oh, I'll fix that up all right. I'll go and see the judge." He was obviously undisturbed by the probability of death which awaited him.

It seems inconceivable that any one could review the life of this man and reach the conclusion that he was normal. By that statement I do not mean that he should be relieved entirely from the responsibility of his crime.

I find that the Binet test, as one of several factors in the determination of the mentality of the individual, is of great value. No one pretends to depend on it or any one test for a diagnosis of feeblemindedness.

DR. WILLIAM HEALY: Feeblemindedness is not necessarily the same thing as mental defect. The committee which in 1912 endeavored to formulate for the American Association for the Study of the Feebleminded a definition of feeblemindedness, that the feebleminded person was one who, by reason of mental defect that had existed from birth or near time of birth, was unable to compete on equal terms with his fellows in the same social environment. The committee also stated that the feebleminded person was one who could not pass the 12 year Binet tests. Since then we have all of us changed our opinion on this matter—that level is too high. But it must be insisted that feeblemindedness connotes certain special disabilities. If a person has a mental age of 10, we will say, and still is able to get along in his environment, he is not to be denominated feebleminded.

In test work with delinquents and criminals one has to insist on the evaluation of test results in the light of the attitude on the part of the person tested. When it comes to the question of defining human responsibility, I confess myself in the light of all these years of experience, as feeling great weakness in making any decision except in the most outspoken cases of deliberate planning of delinquency or in frank cases of mental disease or defect. Responsibility is a metaphysical conception, utilized by the legal profession on a basis of tradition. It involves nothing that can be proved, and it is one of the great stumbling blocks in the way of good work in the criminal courts. Psychiatrists are forced by legal procedure to attempt to answer the problems in these terms, with very little credit accruing in any way. Perhaps murder trials, such as Dr. Walton cites, are rather an exception.

I am convinced that psychiatry has a glorious future, not so much in the mere examination of criminals with the idea of classifying them, but that we may become more efficient in taking care of delinquent persons so that delinquency will be diminished. This is something that we are certain of because the proofs are at hand. By intelligence tests and the study of personalities and behavior trends and of the dynamics of the situation, we can be of some assistance in helping the courts to solve the problem. But I am not at all sure that it will ever be in terms of responsibility.

The present demand for psychiatrists who are really students of delinquency is very interesting. One of the big foundations of New York is going into the problem of delinquency and spending $160,000 a year for five years in order to demonstrate the value of preventive measures. A clinic is being established in New York; some support is being given to the Boston situation; a flying clinic

is being sent out to the courts of other cities; a county in New Jersey is being aided in its problems. A psychiatrist, psychologist and social worker in all these separate endeavors are to work together.

DR. WALTON, in closing: I agree with Dr. Thom in regard to the importance of the intelligence tests, and supposed I had put myself on record as fully appreciating them. It is in such cases as I have reported that they seem to me to fall short. I am glad to adopt the suggestion of Dr. Stearns, and substitute the expression "questionable value" for "no value." The verdict in both these cases was murder in the second degree; the sentence, state prison for life.

## MULTIPLE SCLEROSIS. By DR. E. W. TAYLOR.

Dr. Taylor reviewed the papers on multiple sclerosis presented at the December meeting of the Association for Research in Nervous and Mental Diseases. (Many of these appear in this issue of the ARCHIVES.)

## THE SOCIETY FOR MENTAL HYGIENE. By DR. C. MACFIE CAMPBELL.

The daily papers have been using the term "mental hygiene." Parlor meetings have been held in order to bring about an interest in this subject and it seems to be in danger of becoming a popular topic of conversation. It may be worth while to study the close relationship between the work of a volunteer organization in mental and nervous disorders and the work of groups of specialists. One must keep in mind that the social conditions under which patients live determine something of the symptomatology of the disorder and that various factors which may not be taken into account in ordinary laboratory investigations may be of considerable scientific importance. Insanity could not be studied accurately until the chains of the insane were struck off. A great many of the phenomena they presented were due to irritation by cruel attendants, physical conditions, abuse and neglect, rather than to any intrinsic nervous disorder. Medical research and the utilization by the public of medical knowledge must always go hand in hand if we are going to make progress in improving the health of the community. If we are going to have a clean water supply and make conditions as hygienic as they ought to be, we must have a popular interest in such matters, and in order that popular interest may have the thorough endorsement of the responsible medical workers. Those not technically familiar with a health situation will naturally ask those who are acquainted with it whether a movement is a solid, intelligent public health movement, or whether it is more or less an ill-balanced and sentimental philanthropic movement. So one may bring up two questions: 1. Is the field adequately prepared by mental hygienists? 2. Is there any necessity for a volunteer organization; is the field not sufficiently covered by federal and state authorities?

The field of mental hygiene is much wider than is generally realized. Psychiatry in the past has dealt too exclusively with the end products or the more severe types of mental disorder, and it is our place to put before the medical student a better perspective with regard to mental disorders. We deal with incipient cases and emphasize to our students the necessity of the early recognition of symptoms. The field of mental disease which is represented by the severe cases of so-called insanity is in many places adequately covered by the state. Within the last fifty or seventy-five years the state has recognized its responsibility in caring for patients with serious cases of mental

disorder; not all states, however, for there are many which offer inadequate care although there may be abstract recognition of state responsibility.

For many patients with mild cases of mental disorder, who hesitate to go to a state hospital, of whom physicians in general say "It is just a nervous breakdown," and for whom they recommend merely rest and palliative treatment, there is inadequate provision. Except in a few large centers that type of person does not receive the hospital care which people with any other type of disease receive. That situation is a matter of great importance to the community because it is at that stage of the disorder that most can be done, and there is the greatest hope of curability. A large number of cases are never regarded as mental disorders; for instance, cases of nervous invalidism, heart cases, patient with gastro-neuroses who haunt the gastro-intestinal clinics, genito-urinary invalids who haunt the genito-urinary clinics; these patients are apt to be considered nuisances, and there is no organization in many large hospitals for their definite treatment. In addition, therefore, to cases of incipient mental disorder, and mental cases masquerading under forms referred to, we have other forms of mental disorder represented by the alcoholic patient, the prostitute and those concerned in other social problems. These groups represent a problem in mental hygiene, a problem of great medical interest and, from the point of view of the community, of great social and economic importance

In the school system, through which all the children of the community pass, we are trying to raise the general health of the public by attention to the teeth and tonsils, but it is as important to give attention to nervous habits, the development of faulty moods, to reactions, such as seclusiveness and sex habits. Going back to children of the preschool age one will find an early stage of the same problem.

To deal with this wide field may seem too big a task, but with each one of these topics one can take very practical steps. In the care of incipient mental disorders there can be not only state outpatient clinics, but clinics associated with all the general hospitals and some sort of local organization through the districts whereby the average person will be assured of a fairly decent examination. Dr. Healy is showing what can be done with delinquency. For other social problems there are a great many organizations but very few have any insight into the principles of mental hygiene, and some coordinating organization is required. A central organization could teach those responsible for educating pupils the importance of these aspects of mental health, and urge that mental hygiene be taught in the normal schools. We can arrange that school physicians have some experience in the psychopathology of childhood and that school nurses have as a part of their training some experience with the same disorders. Dr. Thom at one clinic sees mothers of children of preschool age, and various minor disorders are brought to him. There are two agencies at present in the field which we ought to support vigorously: the Massachusetts Society for Mental Hygiene and the parent society, the National Committee for Mental Hygiene. The present campaign in Boston is to put the relevant data before those who are able financially to support this very important work.

## RESOLUTIONS ON THE DEATH OF WALTER CHANNING, M.D., LL.D.

The following resolutions were read and adopted:

To the members of the Boston Society of Psychiatry and Neurology, both individually and collectively, the death of Dr. Walter Channing, its founder and one of its most valued members, comes with a peculiarly deep sense of

loss. It is given only to men of far sight and unusual powers of mind to serve the cause of humanity as did Channing by initiating and furthering large and practical public measures for the benefit of the insane and feebleminded.

He died at his home in Brookline on Nov. 23, 1921, at the age of 72. He came of distinguished ancestry and was born in Concord, Mass. He was educated at the Chauncy Hall School and the Massachusetts Institute of Technology, and began the study of medicine at the College of Physicians and Surgeons in New York and the Harvard Medical School, later becoming an intern in the Massachusetts General Hospital. Then began his career as a practical psychiatrist by service as assistant physician in certain state hospitals. In 1879, he established his widely known and successful sanatorium in Brookline, now in Wellesley.

He was from the first a frequent contributor to medical and other journals, and became a consultant and medical expert of high repute testifying, among other prominent cases, in that of Guiteau, the slayer of President Garfield.

He was a member of the American Psychiatric and American Neurological Associations, and was the founder of the Department of Mental Diseases of the Boston Dispensary, and professor of mental diseases in Tufts Medical College, where he received the degree of LL.D. in 1900.

It was, however, in his more public work that his remarkable capacity as organizer, planner and adviser found full scope. He was foremost in setting on foot measures which resulted in the formation of the then State Board of Insanity. In securing legislation which resulted in placing the dependent insane of Boston, formerly city charges, under state care he was a large factor, and he was a powerful influence in shaping the subsequent reorganization of the Boston State Hospital. In the establishment of the Boston Psychopathic Hospital also, he was one of the prime movers. He could be relied on to inform and mold professional and public opinion in behalf of any good measure or policy, and had surprising success in turning all interests into helping to pass the laws required to meet these changes.

His great interest in all matters pertaining to the insane and feebleminded, and his unfailing zeal and persistence in every effort to promote their welfare brought him constantly during many years into close contact with state and institutional officers responsible for their supervision. His advice was most helpful and always impersonal and altruistic.

In these general relations the real Channing was not always revealed. Dr. Copp, formerly the executive officer of the Board of Insanity, writes: "I came really to know him in our more intimate relationship while he was chairman of the trustees of the Boston State Hospital, during the period of its transition from a municipal to a state institution, its reorganization in adaptation to the new status, the study of its development and especially the planning of the Boston Psychopathic Hospital. Here were revealed the sympathy, self-effacement, good judgment and unswerving adherence to right policies, principles and methods of administration which made it a joy and inspiration to work with him. His great forcefulness sometimes obscured the warmth and friendliness of his nature. It is one of the deep satisfactions of my life to have known him and enjoyed his friendship."

As a citizen, Channing was equally enterprising and valuable to the town of Brookline in promoting lasting educational improvements and public health measures.

He was a man of calm exterior but superabundant energy. Although somewhat cold and aloof in manner, he formed warm friendships and possessed a

lively sense of humor. He was unusually quick to recognize and applaud worth in others whether of character or achievement, and invariably ready with active help or counsel to his fellow workers. His private charities were many. In short, it may truthfully be said of Channing that in his life and work

". . . he did with cheerful will
What others talked of while their hands were still."

HENRY R. STEDMAN,
G. ALDER BLUMER,
HERBERT B. HOWARD,
Committee.

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## PHILADELPHIA NEUROLOGICAL SOCIETY

*Regular Meeting, Jan. 27, 1922*

GEORGE WILSON, M.D., *President*

### SACRALIZATION OF THE FIFTH LUMBAR VERTEBRA WITH SPINAL SYMPTOMS. DR. ALBERT GORDON.

Attention is called to the sacralization of the fifth lumbar vertebra as a cause of lumbosacral pain. The second ossification of the vertebrae is the direct cause of the sacralization which may appear as early as at the age of 5 or as late as at the age of 48. The clinical picture consists chiefly of pain in the lumbar region with stiffness and deviation of the spine. In a certain group of cases there is also secondary involvement of the roots and of the spinal cord.

An example of such an occurrence is presented. In addition to the pain in the back, stiffness and kyphosis, the patient has sharp pain in the lower extremities and markedly increased knee and extensor plantar reflexes. The interesting points about this case are: uneven distribution of the sacralization, more on one side than on the other; the onset of the painful phenomena at the mature age of 26; and involvement of the roots and spinal cord.

### A CASE OF TABES DORSALIS WITH CHARCOT JOINTS OF THE SPINE AND MARKED WASTING OF THE MUSCLES OF THE RIGHT LEG. DR. S. F. GILPIN.

The patient, a white man, aged 51 years, had a good family and past history, with the exception of a chancre twenty years ago. He strained his spine by lifting one year ago and attributed his present trouble to that injury. His right leg was much smaller than the left and showed marked muscular atrophy. Physical examination showed the classical signs of tabes.

The case is interesting because of the deformity of his spine and the muscular atrophy in the right leg. Roentgen-ray examination showed marked deformity of the fifth lumbar and to some extent of the fourth lumbar vertebra and apparently overproduction of bone. This is the third case of Charcot joint of the spine observed within one year. An interesting question arises as to the cause of the atrophy of the muscles of the right leg. Does he have a separate anterior horn lesion in the lumbar cord or is this overproduction of bone exerting pressure on the nerve roots?

DISCUSSION

DR. WILLIAM G. SPILLER: It is noteworthy that three cases of tabes with arthropathy of the spinal column have occurred within a short time at the Jefferson Hospital. Rare cases sometimes occur within short periods of time, but it should not be thought that tabetic arthropathy of the spinal column is common. I reported a case of this kind twenty years ago (Arthropathy of the vertebral column in tabes, *American Medicine*, Nov. 1, 1902).

## RAPIDLY DEVELOPING COMPLETE BLINDNESS AND DEAFNESS ACCOMPANIED BY MENTAL IMPAIRMENT PRODUCED BY BRAIN TUMOR. Patient presented by DR. EDWARD A. STRECKER.

A widow, 55 years old, the mother of two children, aged 29 and 30, had measles twice during childhood; smallpox at the age of 3, and scarlet fever at 18. Ten years ago a herniotomy was performed and at the same time a uterine tumor (nature unknown) was removed. The climacteric was accomplished three years ago.

About one year ago the patient began to have dizzy attacks during which she fell. At the same time she complained of pain in the eyes, and an ophthalmologist reported fairly good vision and normal eye-grounds, but thought there was incipient cataract. About six months ago the patient began to complain of dimness of vision which in two weeks progressed to absolute blindness. A month later there was difficulty in hearing and in four weeks there was complete deafness. There was no history of headache or vomiting.

Physical examination revealed total blindness. The eyes were examined by Dr. G. E. deSchweinitz and Dr. Wm. T. Shoemaker. The pupils were about 4.5 mm., stiff to light, but apparently there was no interference with the ocular movements. There was bilateral choking of the dsks, amounting to 4 or 5 diopters, the swelling beginning to subside with evidence of nerve atrophy. The patient was deaf in both ears. She did not respond to tests for smell or taste but apparently enjoyed her food. There was a weakness of the left side of the face with a questionable sensory diminution on the same side. Though it was difficult accurately to test the patient, there seemed to be a tendency to fall backward and to the left. Unfortunately, the inability of the patient to cooperate prevented satisfactory neurologic examinations.

Dr. Fisher made the following otoligc report: There was no response on the left side to douching with cold water at 68 or hot water at 114 F. There was some response on the opposite side to cold water. The neuro-otologic examination seemed to indicate involvement of the left cerebellopontile angle.

On Dec. 26, 1921, there was a convulsion, the only one which has ever occurred. Unfortunately, I did not witness this convulsion but the night nurse made the following report: "At 9 p. m. the patient was up and voided a large quantity of dark, reddish colored urine. She seemed about the same as usual excepting that she requested me to press my hands against her head as though she were having a headache. Fifteen minutes later she was found moaning and with the entire body twitching. She had turned on the right side which is unusual as she always sleeps on her back. Twitching of the arms continued, but became less marked in the legs. It was present on both sides. When the patient was turned there was projectile vomiting; the vomitus was dark brown and had an offensive odor. The pupil of the right eye was turned upward and apparently slightly to the right during the convulsion. The entire convulsion

lasted twenty-five minutes." There was no previous instance of vomiting with the exception of an attack accompanied by nausea which followed an injection of morphin.

The laboratory reports showed a trace of albumin and a few hyaline and granular casts in the urine. The blood count and smear were not remarkable. The Wassermann tests of the blood and spinal fluid were negative. The direct pressure of the fluid was twice the normal; the Nonne, Noguchi and Ross-Jones tests were all four plus, and there were never more than two cells. The roentgenograms were not very satisfactory on account of the lack of cooperation of the patient; the report states that there was apparently considerable abnormality about and posterior to the sella. The anterior clinoids were very well shown, but there was no evidence of the posterior. There was considerable lack of density at the base just posterior to this area.

Before her admission to the hospital in November, 1921, the family gave the following account of her mental condition: "Three months ago her son brought a strange man to the house. The patient disliked and feared him. After he had gone, she insisted that he was still in the house and said that he beat and kicked her. She told the neighbors that her family abused her and starved her. She pounds on the walls and screams 'murder' from the windows and front porch. She is resistive, antagonistic, and stubborn and strikes at every one who goes near her; she delivers angry tirades at members of the family, and if she cannot have her own way, becomes very much excited. She is not destructive or untidy, and she has a good appetite and sleeps well. She becomes confused as to her whereabouts at times. She thought she was on the porch when she was in bed and attempted to climb the bed post. She threatened to kill herself if she were taken to a hospital; she was brought today by force." Since her admission to the hospital such marked symptoms had not been noted. It, of course, seemed difficult to estimate her mental reactions. There seemed to be confusion and at times disorientation. Occasionally she quarreled with and scolded some of the members of her family, and it is possible such conduct was dictated by the vague paranoid trend. For the last two weeks she has seemed quite dull and stupid and at times has been untidy. More recently the patient's judgment of spatial relations has been faulty. For instance, several times she apparently did not realize that her position had been changed from a sitting to a reclining one. Again she frequently complained that the position of the bed had been reversed.

### DISCUSSION

Dr. T. H. Weisenburg: The symptoms presented in the patient are indicative of a cerebellar lesion which has extended into the pontile angle on both sides involving the eighth nerves on both sides, and in addition the facial nerve on the left.

The history undoubtedly points to a brain tumor as indicated by the gradual development of the choked disk with loss of vision. The involvement of both eighth nerves is shown by the gradual loss of hearing and the history of dizzy attacks, during which she fell.

My examination demonstrated that the patient had a tendency to stagger backward, chiefly to the left. There is also a weakness of the left seventh nerve. Asynergy could not be tested for in either the upper or the lower limbs, but the falling backward and to the left indicated that the asynergy was chiefly in the trunk.

It seems to me that the best explanation of the symptoms in this patient is given by a tumor in the fourth ventricle which has extended into both angles involving both eighth nerves.

About fifteen years ago, with Dr. Mills, I studied a patient with almost similar symptoms. She had disturbance and later loss of sight and hearing with involvement of the seventh nerve on both sides, instead of on one side as in this patient. She also had asynergy, chiefly of the trunk for she always staggered backward. Pathologic examination showed a tumor filling up the entire fourth ventricle in which there was extension into both cerebellopontile angles involving both seventh and eighth nerves.

Dr. John G. Wilson, Norristown: Several years ago I saw a patient who had severe headache for four or five days, with no mental symptoms, but who in the course of three or four days gradually became completely blind. Examination of the fundus showed a double choked disk, but two or three days after this she had a vomiting spell and discharged three or four ounces of pus from her nose, after which the symptoms disappeared.

Dr. Charles K. Mills: Doubtless the case just reported is one of tumor, either frontal or cerebellar, perhaps of the lower inferior surface of the cerebellum. What impressed me was that the patient not only had double choked disk, causing blindness, but that she had bilateral deafness which might possibly be due to a cause similar to that producing her blindness. Some years ago I called attention to the possibility of having what might be termed an eighth nerve or auditory choked disk. I see no reason why this might not occur when one considers the course of the eighth nerve from the cochlea and semicircular canal through the internal auditory meatus to the brain stem. An objection to the structural pathogenesis suggested by Dr. Weisenburg is that it seemed almost impossible that the tumor should extend so as to involve the tissues of the floor of the fourth ventricle and not produce other symptoms than those which were mentioned.

## A STUDY OF HEREDITY IN EPILEPSY, BASED ON ONE THOUSAND FOUR HUNDRED AND FORTY-NINE CASES. Dr. C. W. Burr.

This paper will be published in full in a future number of the Archives of Neurology and Psychiatry.

### DISCUSSION

Dr. J. Hendrie Lloyd: The subject of heredity is so much involved that we ought to recognize the fact that we cannot know much about it in reference to disease. The study of heredity through one or two generations does not really throw much light on it; I think this is proved by a simple consideration of the mendelian laws. What can we tell about heredity? There is probably not a man in the room who knows accurately the diseases that his four grandparents died of. Now when we go back to the generation before that, the great grandparents, we are in absolute ignorance. If you multiply every generation by two, as you must—for every man has two parents, four grandparents, eight great grandparents, sixteen great, great grandparents and so on—by the time you have gone back twenty generations you have had one million ancestors. You can take a lead pencil and figure this out for yourselves. How is it possible in that vast sum of ancestors, who have disappeared into the empyrean, to tell what diseases they had?—gout, rheumatism, syphilis,

epilepsy, insanity, alcoholism, tuberculosis, cancer and what not? If they had transmitted their diseases to their descendants how would it be possible for any of us to be alive? There is something in the whole subject that escapes us. We must have some ability to throw off these inherited traits from our ancestors, possibly by a process of natural selection in the chromosomes. It is a struggle for existence. I agree with Dr. Burr in regard to syphilis. This is not a hereditary disease; it is a congenital disease. Heredity is only that which is transmitted through the germ plasma. Syphilis is transmitted by a spirochete. Even if it got into an ovum, this would not be an instance of hereditary disease, but an evidence of transmitting a disease from the mother to the ovum, by a spirochete. But it is doubtful whether an ovum thus invaded could develop. David Starr Jordan has recently written a paper on heredity in which he attempts to prove that there are probably several million people now living who are descended from the Emperor Charlemagne. He went to the extent of giving the geneologies of Abraham Lincoln, of Grover Cleveland and Theodore Roosevelt, as descendants of Charlemagne. I would not be surprised if many in this room were descendants of Charlemagne. If Charlemagne could transmit by simple arithmetical progression in every generation, there had been time for him to have twenty million descendants. This seems like a reductio ad absurdum, but it illustrates the difficulties of the problem.

DR. CHARLES S. POTTS: Dr. Burr's paper is a good presentation of the subject. I was glad to hear what Dr. Burr has said about the influence of alcohol in the parents as a cause of epilepsy. Several years ago the idea occurred to me that if half that was blamed on alcohol were true, considering the alcoholic habits of our ancestors, a great majority of us should be either epileptic or imbeciles.

## A CASE OF UNILATERAL OPTIC ATROPHY AND CONTRALATERAL HEMIPLEGIA RESULTING FROM OCCLUSION OF THE CEREBRAL VESSELS. DR. N. W. WINKELMAN.

On July 1, 1921, a white man, aged 61 years, whose family history was negative, suddenly dropped to the floor unconscious. He was in bed three weeks and during this time he could not talk and could not move the right side of his body, including the face. His wife noticed that his left eye was turned outward. Since that time he had made slight improvement, and he soon found that his left eye was completely blind, a condition which he is absolutely sure was not present prior to his "stroke." He is now motor aphasic, and walks with a distinctly right hemiplegic gait. He shows marked arteriosclerosis. His pupils are irregular; the right reacts quickly but the left is stationary to light, though the consensual light reaction is retained. There is absolute blindness in the left eye. He is able to read words and letters of large size. The reflexes on the right are exaggerated, with the Babinski sign and ankle clonus present. There is no loss of stereognosis. He is able to obey simple commands, though there is definite lack of ability to carry out complicated commands. His memory is much impaired, but he is able to find his way around the neighborhood. The eye report by Dr. Langdon is as follows: "The upper branch of the central artery of the left eye is patulous but is very irregular in caliber. The inferior branch is nothing but a glistening fibrous band, apparently without blood in it."

The diagnosis, therefore, is an incomplete obstruction of the left internal carotid artery at the point where the ophthalmic artery is given off and occluding that artery also.

DISCUSSION

Dr. W. B. Cadwalader: In 1912 I presented a patient before this Society with unilateral optic atrophy and contralateral hemiplegia with aphasia caused by occlusion of certain cerebral vessels. So far as I know, Dr. Winkelman's case is only the second one ever recorded in this country and the condition, therefore, must be exceedingly rare. It can be easily explained by assuming that an embolism has separated, one portion passing into the ophthalmic vessel or into the central artery of the retina producing optic atrophy secondarily on the same side, and another portion being carried into the middle cerebral vessel of the same side, causing softening of the brain that produced aphasia and hemiplegia on the opposite side of the body. That an embolism can be divided into two portions and occlude two separate cerebral vessels simultaneously might seem to be far-fetched. However, this was actually found at postmortem examination in such a case by Growers, of London, to which Dr. Winkelman will refer in the report on his patient.

## AN EPILEPTIC WOMAN AND HER SIXTEEN CHILDREN.

This paper was read by Dr. N. S. Yawger.

# Book Reviews

LE REFLEX PILOMOTEUR. ETUDE ANATOMO-CLINIQUE SUR LE SYSTEME SYMPATHIQUE. Avec 74 Figures et 12 Planches En Noir Et En Couleurs. André-Thomas Médecin de l'Hôpital Saint-Joseph, Vice-président de la Société de Biologie. Pp. 242. Price, 25 francs. Paris: Masson et Cie, 1921.

During the war Dr. André-Thomas examined many wounded soldiers suffering from lesions of the spinal cord and other parts of the nervous system and in these cases studied the pilomotor reflexes. In order properly to interpret such clinical observations it is necessary to have a clear conception of the anatomy and physiology of the sympathetic nervous system and particularly of the arrangement of the neurons which innervate the smooth muscle of the hair follicles. The first chapter of the book is devoted to such fundamental considerations as the following: the smooth muscle of the skin, the anatomy of the sympathetic nervous system, the histology of the sympathetic ganglions, the visceral efferent cell column of the spinal cord, and the physiology of the pilomotor reactions; and presents a good summary of existing information on the topics treated. On disputed points the author follows closely the work of Cajal and Langley and gives in some detail the results of the latter investigator's epoch making study of the pilomotor innervation in the cat.

In the second chapter the author deals with the pilomotor reflexes in man and with the technic of eliciting them. Cold was found to be the most effective stimulus, though heat, electricity and mechanical stimuli also were effective. Tickling or rubbing the hand lightly over the skin or firmly grasping the skin and underlying muscles are efficient mechanical stimuli. When the excitation is unilateral the pilomotor reflex is unilateral. After tickling or pinching the nape of the neck, goose flesh appears over the corresponding half of the body. The superior part of the body reacts first, the phenomenon extending to the lower part of the trunk and the inferior extremity. If the reflex is ephemeral, the reaction may have disappeared from the arms and upper part of the body when at its height over the lower part of the trunk and the leg. Since the response is least easily evoked in the skin of the head and neck, it may be necessary to prolong and reinforce the stimulus in order to make sure that these parts will participate. When the excitation is bilateral and symmetrical the reaction is also bilaterally symmetrical.

In sensitive persons an undiminished reflex may be obtained many times with the same stimulus. But often after two or three trials the reaction becomes feeble or entirely fails to appear. Light stimuli do not always provoke a complete unilateral reflex. Stroking the skin of the thorax may cause a reaction limited to that side of the thorax and the corresponding arm. In the same way stroking the abdominal wall below the umbilicus may cause a reaction over that side of the abdomen and the corresponding leg.

In Chapter 3 are presented the results of examination of wounded soldiers with transverse lesions of the spinal cord. It contains reports of twenty-nine cases in which he was able to check his clinical observations against the findings at necropsy and of twenty-three more in which the data are purely clinical. These observations constitute an important addition not only to clinical neu-

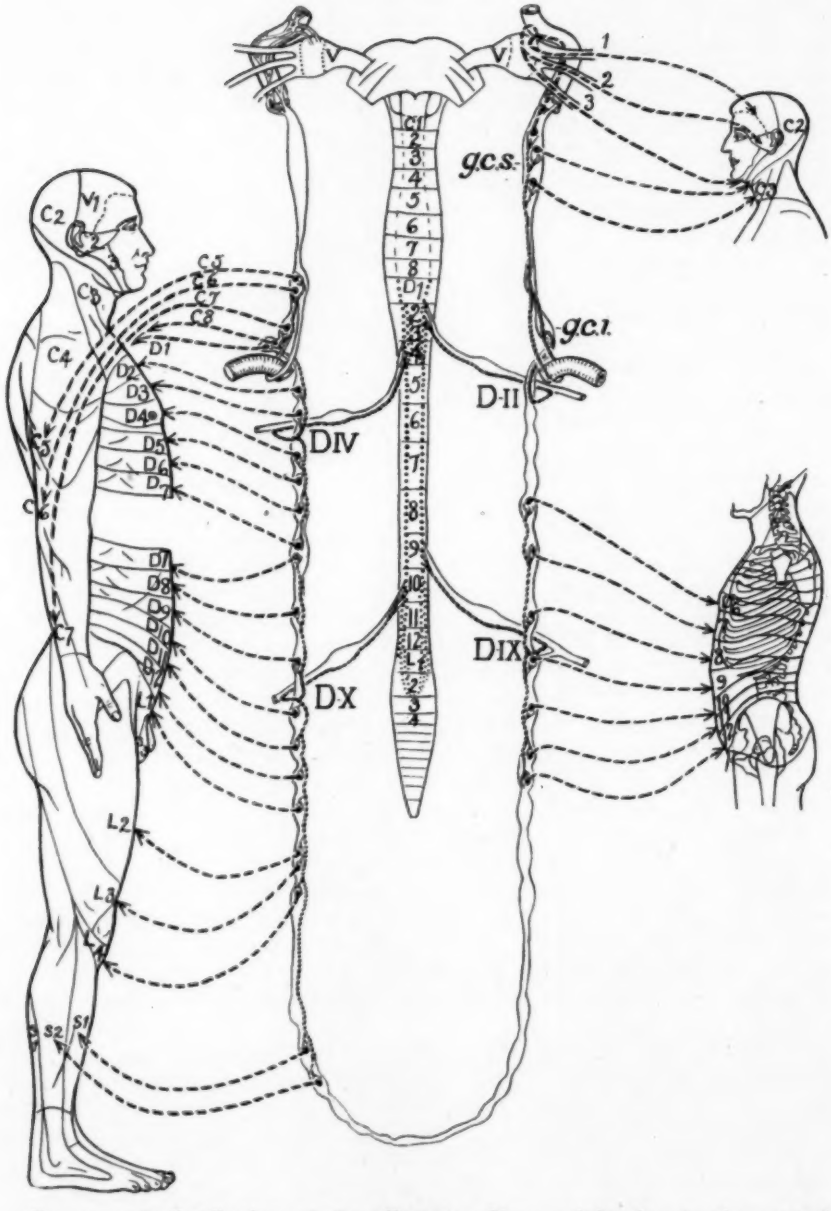
rology but also to the anatomy and physiology of the sympathetic system and furnish data by the use of which the author has been able to construct a scheme of the arrangement of the pilomotor neurons in man.

Chapter 4 is devoted to a systematic examination and interpretation of the observations presented in the preceding chapter. The conclusions reached from the study of patients with transverse lesions of the cord are in close agreement with those of Langley. That investigator stimulated the ventral roots of each of the spinal nerves in the cat and noted the extent of the resulting pilomotor response. André-Thomas noted the level at which the pilomotor reflex was interrupted by transverse lesions of the spinal cord. His conclusions concerning the distribution of the pilomotor neurons in man are summarized in the accompanying table. In order to make the significance of this table clear we also reproduce in simplified form an illuminating diagram illustrating the course and distribution of the pilomotor fibers originating in the second, fourth, ninth and tenth thoracic segments of the spinal cord.

Like other visceromotor fibers of the thoracicolumbar outflow the preganglionic pilomotor fibers take origin from the intermediolateral cell column of the thoracic and first two lumbar segments of the spinal cord. They run through the ventral roots and white rami to the sympathetic trunk within which they run up or down for varying distances and end within the ganglions of the trunk. The fibers from a given spinal cord segment are distributed to several segmental sympathetic ganglions. (The superior cervical, *g.c.s.*, and inferior cervical ganglions, *g.c.i.*, each represent several segmental ganglions fused together.) Within the ganglions of the sympathetic trunk the preganglionic fibers enter into synaptic relations with postganglionic neurons. The fibers arising from these neurons of the second order relay the impulses to the smooth muscle of the hair follicles. They run from the segmental sympathetic ganglions by way of the gray rami communicantes to the spinal nerves of the corresponding segment and are distributed through these nerves to the respective dermatomes. For example, the preganglionic pilomotor fibers from the first three thoracic segments of the cord run upward in the sympathetic trunk to the superior cervical sympathetic ganglion, whence the impulses which they carry are relayed by postganglionic fibers along the trigeminal and second and third cervical nerves to the skin of the head and neck.

Transverse section of the spinal cord arrests the transmission of impulses within the cord from segments above to segments below the lesion and vice versa. Stimulation of the skin above the line of anesthesia causes erection of the hairs in the dermatomes receiving pilomotor impulses from the segments of the cord above the lesion. Because these cord segments are still under the influence of the brain the author designates these reactions as encephalic reflexes.

Some time, varying from several days to a few weeks after the injury, the segments of the spinal cord below the lesion take on a new activity independent of the higher centers; that is, they show spinal automatism. The pilomotor responses, which can then be obtained by stimulating the skin below the line of anesthesia and which must be mediated entirely by those segments of the spinal cord which are cut off from the brain, are designated as spinal reflexes. These spinal pilomotor reflexes are of value in fixing the extent and lower limit of the lesion. The upper limit of the lesion is of course determined by the line of anesthesia and the muscles which are paralyzed. Knowing the dermatomes which are supplied with pilomotor fibers by the various segments of the cord it is possible to form an idea of the lower limit of the lesion by determining the highest dermatome included in the spinal pilomotor reflex.




Course and distribution of the pilomotor fibers originating in the second, fourth, ninth and tenth thoracic segments of the spinal cord.

A few illustrative cases may be cited to show the limits of the skin areas supplied by certain spinal cord segments. A soldier with a complete transverse lesion in the third and fourth spinal cord segments showed an encephalic reflex limited to the face and neck. No response occurred below the cutaneous area supplied by the third cervical nerve. This dermatome, then, represents the lower limit of pilomotor innervation from the second thoracic segment of the cord (D II). In another case with destruction of the fourth thoracic segment an appropriate stimulus applied above the line of anesthesia caused goose flesh to appear over the area on the shoulder supplied by the fourth cervical nerve. In still another case the fifth and sixth segments were destroyed, but the encephalic reflex covered the entire arm and the thorax to the level of the costal arch. From these last two cases it is clear that the fourth thoracic segment must supply the dermatomes from the fifth cervical to the seventh thoracic inclusive (D IV).

GANGLIONS OF THE SYMPATHETIC TRUNK*

| Segments of Spinal Cord | | | Dorsal | | | | | | | | | | | Lumbar | | | | | Sacral | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I | g.c.s. | | | | | | | | | | | | | | | | | | | | | | | |
| II | g.c.s. | | | | | | | | | | | | | | | | | | | | | | | |
| III | g.c.s. | | | | | | | | | | | | | | | | | | | | | | | |
| IV | g.c.s. | g.c.i. | 1 | 2 | 3 | 4 | 5 | 6 | | | | | | | | | | | | | | | | |
| V | ..... | g.c.i. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8? | | | | | | | | | | | | | | |
| VI | ..... | g.c.i. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9? | | | | | | | | | | | | | |
| VII | ..... | g.c.i. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10? | | | | | | | | | | | | |
| VIII | ..... | | | | | | 5 | 6 | 7 | 8 | 9 | 10 | 11 | | | | | | | | | | | |
| IX | ... ..... | | | | | | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 1 | | | | | | | | | | |
| X | ..... | | | | | | 7 | 8 | 9 | 10 | 11 | 12 | | 1 | 2 | 3 | 4 | 5 | 1 | 2 | | | | |
| XI | ..... | | | | | | | 8 | 9 | 10 | 11 | 12 | | 1 | 2 | 3 | 4 | 5 | 1 | 2 | 3 | 4 | 5 | Coccygeal |
| XII | ..... | | | | | | | 9 | 10 | 11 | 12 | | | 1 | 2 | 3 | 4 | 5 | 1 | 2 | 3 | 4 | 5 | 1 |
| I | ..... ..... | | | | | | | | 10 | 11 | 12 | | | 1 | 2 | 3 | 4 | 5 | 1 | 2 | 3 | 4 | 5 | 1 |
| II | ..... | | | | | | | | | 11 | 12 | | | 1 | 2 | 3 | 4 | 5 | 1 | 2 | 3 | 4 | 5 | 1 |

* This table shows the ganglions of the sympathetic trunk in which the preganglionic pilomotor fibers arising from the various segments of the spinal cord terminate. Each of these ganglions sends postganglionic pilomotor fibers to the corresponding dermatome; g.c.s., superior cervical ganglion; g.c.i., inferior cervical ganglion.

In a number of patients in whom the lesion was situated just below the tenth dorsal segment the encephalic reflex covered the entire lower extremity. The upper limit of pilomotor supply from the tenth thoracic segment is given by a case in which the seventh, eighth and ninth thoracic segments were destroyed but in which a stimulus below the line of anesthesia produced a spinal pilomotor reflex extending upward to the seventh thoracic dermatome. From these facts the author concludes that the tenth thoracic segment supplies pilomotor innervation to the skin of the abdomen and lower extremity; that is, to the dermatomes from the seventh thoracic to the second sacral inclusive (D X).

Chapter 5 is devoted to the pilomotor reflexes in such diseases of the spinal cord as transverse myelitis, pachymeningitis, anterior poliomyelitis and syringomyelia.

Chapter 6 deals with the pilomotor reflexes in cases of lesions of the peripheral nerves. If a nerve is injured distal to the point where it receives the fibers of the gray rami communicantes, the smooth muscles of the hair follicles are paralyzed in the cutaneous area supplied by that nerve. If, however, the nerve roots going to form the brachial or lumbosacral plexuses are destroyed within the spinal canal or intervertebral foramina, the pilomotor reactions will not be affected because at this point the roots contain no pilomotor fibers. The presence or absence of pilomotor reactions in the areas of anesthesia resulting from injuries to the roots of the brachial and lumbosacral plexuses is therefore a matter of considerable diagnostic importance in determining the location of the lesion.

In Chapter 7 there are recorded five cases of lesions involving the sympathetic trunk. The symptoms were such as might be inferred from the anatomic course of the pilomotor fibers. Chapter 8 deals with the pilomotor reflexes in patients with brain lesions and in the insane; Chapter 9 with the effect of skin diseases on these reflexes; and Chapter 10 with the exaggeration of these reflexes caused by irritative lesions. The book ends with an account of the nature of the encephalic reflex.

The entire work, with the exception of the introductory chapter, rests on observations made by the author. It covers an entirely new field and contains many new facts some of which may prove to be of considerable clinical importance.

S. W. RANSON.

THE ANATOMY OF THE NERVOUS SYSTEM FROM THE STANDPOINT OF DEVELOPMENT AND FUNCTION. By STEPHEN WALTER RANSON, M.D., PH.D., Professor of Anatomy in Northwestern University Medical School, Chicago. Cloth. Price, $6.50. Pp. 395, with 260 illustrations. Philadelphia: W. B. Saunders Company, 1920.

In this book an excellent presentation is made of the anatomy of the nervous system. The first two chapters are devoted to the origins and functions of the nervous system and the neural tube and its derivatives. The third chapter is concerned with the histogenesis; the fourth with the neurons and neuron chains; the fifth with spinal nerves. From here the various parts of the nervous system, beginning with the spinal cord, are discussed in order.

The manner of discussion is different from that found in the usual anatomy in the sense that the functions of the parts are given in correlation with the anatomic data. This is the logical method of teaching the student anatomy and physiology and is admirably worked out. The physiology in comparison has naturally received only scant attention, but it is given in sufficient detail for the student.

It is difficult to review the various chapters, but there are many features in this work which are not present elsewhere. The book has been so arranged as to facilitate comparative studies of the head of the shark and the brain of the sheep which, as the author points out, are used in many laboratories. Besides, there is an outline for a course in neuro-anatomy.

The illustrations are excellent, many of them original; for example, the dissections of the internal capsule, the corona radiata and the thalamic radiation to the temporal lobe which are the result of the so-called mechanical dis-

sociation, for it has been found that in formaldehyd hardened material bundles of fibers can be followed with ease and the outline of nuclear masses readily determined. The author has already described these dissections in a contribution in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY (Description of Some Dissections of the Internal Capsule, the Corona Radiata and the Thalamic Radiation to the Temporal Lobe **5**:361 [April] 1921).

The manner of the discussion of subjects is very well thought out. For example, in the chapter on the cerebellum there are given in order the development, gross anatomy, morphology, functional localization, the finer anatomy and connections of the cerebellum with the rest of the brain, and finally the histology.

Perhaps some criticism could be directed to the chapter on cortical or cerebral localization. While motor localization is properly stated, nevertheless in one of the succeeding chapters, on page 317, an old illustration by Starr is used, indicating the motor centers, especially in their lower portion, as being partly in the postcentral convolution. Perhaps a better choice of illustration can be made in a subsequent edition. In discussing the visual receptive centers on page 292, the modern conception of the visual localization, as developed by the war literature, has not been taken advantage of. The old classical idea of aphasia is adhered to. It is wise as the author states not to discuss any controversial parts in a book of this sort.

With the exception of these few points, nothing but praise can be given the book. The publishers have done their work well—the paper is good, the text clear and not at all tiresome to the reader. The book can be recommended for the student in anatomy.

FOUNDATIONS OF PSYCHIATRY. By WILLIAM A. WHITE, M.D., with an Introduction by DR. STEWART PATON. Pp. 134. New York and Washington: Nervous and Mental Disease Monograph Series No. 32. Nervous and Mental Disease Publishing Company.

Within the space of this small volume Dr. White has essayed "to formulate a Philosophy of Psychiatry." He discusses the evolution of the psyche, the integration, dynamics and stratification of the organism; psychopathology, the nature of the neuroses and psychoses and the application of the principles formulated to therapy and social organization. Necessarily these are presented in greatly condensed form, and the language is highly technical and often without definition. It is therefore necessary for the reader to possess a fairly intimate acquaintance with the subject.

The earlier chapters are devoted to the concept of psychiatry as the study of "What is the man doing?" With admirable illustrative examples and many well selected quotations from contemporary literature it is shown that man is an integration and not merely the sum of the various organs of which he is built. What he does is a problem of relations between the needs or desires inherent in him as a living organism and the conditions under which he must satisfy those needs. In other words, it is a dynamic or action and reaction (ambivalent) relation, the desire or "wish" being the unit of activity. Instead of sensations which constitute the unit of formal descriptive psychology, affects, representing the cravings of various autonomic segments, are the fundamental motives of behavioristic psychology. Interesting comparisons are made between affect and intellect on the one hand and protopathic and epicritic sensibility on the other. Conditioned reflexes are mentioned incidentally but are not used by the author to any extent in the development of his subject.

The later chapters of the book are practically a résumé of the views of the psychanalytic schools, and a concise description and comparison is given of the views of Janet, Freud, Jung, Adler and Kempf. No allusion is made to the studies of the neuroses which arose during the war. White carries this discussion even into the rôle of psychologic mechanisms in the etiology of many chronic diseases and the "problem why certain etiological factors, for instance, the tubercle bacillus, should attack the lung in one person, the kidney in another, etc." That a study of the personality in any form of disease is essential to the adequate treatment of the man diseased will be conceded by all, but this concerns the practice rather than the foundations of psychiatry.

The keynote of the work, however, is the recognition of the man as a personality, an integrated organism struggling for satisfaction in a social milieu which is itself an integration and not a mere collection of individuals. For this reason the book is worth reading, although it cannot be recommended for the use of students about to begin the study of psychiatry.

ELEMENTS DE PATHOLOGIE MENTALE CLINIQUE ET MEDECINE LEGALE. Par R. BENON, Ancien Interne de la Clinique de Pathologie Mentale et des Maladies de l'Encephale de la Faculté de Médecine de Paris; Médecin du Quartier des Maladies Mentales de l'Hospice Général de Nantes. Avec Préface de M. BALTHAZARD, Professeur de Médecine légale a la Faculté de Médecine de Paris, Membre de l'Académie. Price, 6 francs. Pp. 242. Paris: Librairie Octave Doin, Gaston Doin, Editeur, 8 Place de L'Odéon, 1922.

This is an excellent example of the small elementary medical guides of which the French seem to be fond. Like many of the others it is bound in paper and rather poorly printed on poor paper. But the matter is good.

The work is essentially clinical, based on the author's experience as a teacher, and obviously designed for the beginner. It begins by defining the current terms of psychiatry and then presents mental disorders in symptom groups —a very good method of approach for a book of this kind, for after all it is a group of symptoms which the patient presents to the physician. First, delirium is considered, then dementia, then mania, etc. The symptom is defined, explained and its clinical application presented. The author has attained his desire to present his matter simply, clearly and with precision.

While this little manual can in no wise be considered a medical textbook except as introductory to some more complete work, we know of nothing which would be more satisfactory for the instruction of the more intelligent attendants in hospitals and sanatoriums for the insane.